

9-25-a

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Docket Number S-130-4080C

FILING BY "EXPRESS MAIL" UNDER 37 CFR 1.10

EL034399825US
Express Mail Label NumberSeptember 22, 2000
Date of DepositAddress to: Assistant Commissioner for Patents
Box Patent Application
Washington, DC 20231

UTILITY PATENT APPLICATION TRANSMITTAL AND FEE SHEET

Transmitted herewith for filing under 37 CFR §1.53(b)(1) is a **divisional** of prior Application No. 09/001,982, filed December 31, 1997.

Applicant (or identifier): BOSCH ET AL.

Title: GENES ENCODING HYBRID *BACILLUS THURINGIENSIS* TOXINS

Enclosed are:

1. ☒ Specification (Including Claims and Abstract) - 92 pages
 2. ☒ Drawings - 7 sheets (*formal*)
 3. Declaration and Power of Attorney
 - a. ☐ Newly executed (original or copy)
 - b. ☒ Copy from a prior application (signed or with indication that original was signed)
 - i. ☐ Deletion of Inventors
Signed statement attached deleting inventor(s) named in the prior application
 4. ☒ Incorporation By Reference
The entire disclosure of the prior application, from which a copy of the Declaration and Power of Attorney is supplied under Box 3b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.
 5. ☐ Microfiche Computer Program (appendix)
 6. Nucleotide and/or Amino Acid Sequence Submission
 - ☒ Computer Readable Copy
 - ☒ Paper Copy
 - ☒ Statement Verifying Identity of Above Copies
 7. ☒ Preliminary Amendment
 8. ☐ Assignment Papers (Cover Sheet & Document(s))
 9. ☐ English Translation of
 10. ☒ Information Disclosure Statement
 11. ☐ Certified Copy of Priority Document(s)
 12. ☒ Return Receipt Postcard
 13. ☒ Other: Bibliographic Data Sheet
- ☒ The right to elect an invention or species that is different from that elected in parent Application No. 09/001,982 in the event of a restriction or election of species requirement that is identical or substantially similar to that made in said parent application is hereby reserved.

Filing fee calculation:

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| Multiple Dependent Claim Fee (\$ 260) | | | | | | | \$ | |
| Foreign Language Surcharge (\$ 130) | | | | | | | \$ | |
| | For | Number Filed | | Number Extra | | Rate | | |
| Extra Claims | Total Claims | 29 | -20 | 9 | x | \$ 18 | = | \$ 162 |
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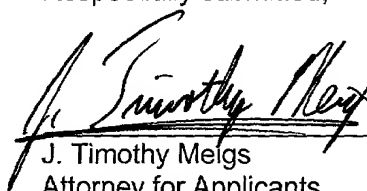
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Date: September 22, 2000

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CORRESPONDENCE INFORMATION

Correspondence Customer Number:: 022847

APPLICATION INFORMATION

Title Line One:: Genes Encoding Hybrid Bacillus thuringie
Title Line Two:: nsis Toxins
Total Drawing Sheets:: 7
Formal Drawings?: Yes
Application Type:: Utility
Docket Number:: S-130-4080C
Secrecy Order in Parent Appl.?: No

CONTINUITY INFORMATION

This application is a:: DIVISION OF
> Application One:: 09/001,982
Filing Date:: 12-31-1997

Which is a:: CONTINUATION IN PART OF
>> Application Two:: 08/602,737
Filing Date:: 02-21-1996
Patent Number:: 5736131

Which is a:: 371 OF
>>> Application Three:: EP94/02909
Filing Date:: 09-01-1994

PRIOR FOREIGN APPLICATIONS

[illegible]

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

BOSCH ET AL.

APPLICATION NO: TBA

FILED: SEPTEMBER 22, 2000

FOR: GENES ENCODING HYBRID *BACILLUS THURINGIENSIS* TOXINS
(AS AMENDED)

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Applicants respectfully request that the above-captioned application be amended as follows in advance of examination:

IN THE SPECIFICATION

Please change the title to -- Genes Encoding Hybrid *Bacillus thuringiensis* Toxins --.

Please replace the continuing data beneath the title with the following: -- This application is a division of application no. 09/001,982, filed December 31, 1997, which is a continuation-in-part of application no. 08/602,737, filed February 21, 1996, now U.S. Patent No. 5,736,131, which is a § 371 of international application no. PCT/EP94/02909, filed September 1, 1994. The aforementioned applications are incorporated herein by reference. --.

IN THE CLAIMS

Please cancel claims 1-16, 18-20, 29-31, 35-40 without prejudice or disclaimer.

Please amend claims 17 and 21 as follows:

17. (Amended) An isolated DNA molecule encoding [a protein that comprises the amino acid sequence of the hybrid toxin fragment of claim 1.] a polypeptide comprising an insecticidal *Bacillus thuringiensis* hybrid toxin fragment, comprising:

- a) at a C-terminus of said fragment, domain III of a first Cry protein; and
- b) at an N-terminus of said fragment, domains I and II of a second Cry protein different from the first Cry protein.

21. (Amended) An isolated [*Bacillus thuringiensis* hybrid toxin fragment] DNA molecule according to claim [1] 17, wherein said hybrid toxin fragment binds to a binding site in an insect gut that is different than the site bound by said first Cry protein.

Please add new claims 41-57 as follows:

- 41. An isolated DNA molecule according to claim 17, wherein said first Cry protein is CryIC.
- 42. An isolated DNA molecule according to claim 17, wherein said second Cry protein is selected from the group consisting of CryIA, CryIE, and CryIG.
- 43. An isolated DNA molecule according to claim 42, wherein said second Cry protein is CryIA.
- 44. An isolated DNA molecule according to claim 42, wherein said second Cry protein is CryIE.
- 45. An isolated DNA molecule according to claim 42, wherein said second Cry protein is CryIG.
- 46. An isolated DNA molecule according to claim 17, wherein said first Cry protein is CryIC, and wherein said second Cry protein is CryIA, CryIE, or CryIG.
- 47. An isolated DNA molecule according to claim 17, wherein said C-terminus comprises the sequence from amino acid position 454 to position 602 of SEQ ID NO:2.
- 48. An isolated DNA molecule according to claim 17, wherein said C-terminus comprises the sequence from amino acid position 478 to position 602 of SEQ ID NO:2.
- 49. An isolated DNA molecule according to claim 17, wherein said insecticidal *Bacillus thuringiensis* hybrid toxin fragment comprises an amino acid sequence at least 90% similar to amino acids 1-620 of SEQ ID NO:6.
- 50. An isolated DNA molecule according to claim 17, wherein said insecticidal *Bacillus thuringiensis* hybrid toxin fragment comprises an amino acid sequence at least 90% similar to amino acids 1-627 of SEQ ID NO:8.

51. An isolated DNA molecule according to claim 17, wherein said insecticidal *Bacillus thuringiensis* hybrid toxin fragment comprises an amino acid sequence at least 90% similar to amino acids 1-602 of SEQ ID NO:12.
52. An isolated DNA molecule according to claim 17, comprising a nucleotide sequence that hybridizes to nucleotides 1-1860 of SEQ ID NO:5 under the following set of conditions: hybridization at 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄ pH 7.0, 1 mM EDTA at 50°C; wash with 2X SSC, 1% SDS, at 50°C.
53. An isolated DNA molecule according to claim 17, comprising a nucleotide sequence that hybridizes to nucleotides 1-1881 of SEQ ID NO:7 under the following set of conditions: hybridization at 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄ pH 7.0, 1 mM EDTA at 50°C; wash with 2X SSC, 1% SDS, at 50°C.
54. An isolated DNA molecule according to claim 17, comprising a nucleotide sequence that hybridizes to nucleotides 1-1806 of SEQ ID NO:11 under the following set of conditions: hybridization at 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄ pH 7.0, 1 mM EDTA at 50°C; wash with 2X SSC, 1% SDS, at 50°C.
55. An isolated DNA molecule according to claim 17, comprising a nucleotide sequence that is at least 90% identical to nucleotides 1-1860 of SEQ ID NO:5.
56. An isolated DNA molecule according to claim 17, comprising a nucleotide sequence that is at least 90% identical to nucleotides 1-1881 of SEQ ID NO:7.
57. An isolated DNA molecule according to claim 17, comprising a nucleotide sequence that is at least 90% identical to nucleotides 1-1806 of SEQ ID NO:11.

REMARKS

The title has been changed to more accurately reflect what is being claimed. The continuing data has also been updated. Claims 1-16, 18-20, 29-31, 35-40 have been canceled; claims 17 and 21 have been amended; and new claims 41-57 have been added. Thus, the pending claims are 17, 21-28, 32-34, and 41-57.

Applicants note that claim 17 (now the sole independent claim) has been amended to recite the encoded hybrid *Bt* toxin using language identical to that in allowed claim 1 of parent application no. 09/001,982. Thus, it is believed that claim 17 of the instant application is allowable as amended. The

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HYBRID TOXIN

This application is a continuation-in-part of application serial no. 08/602,737, filed February 21, 1996, which is a 371 of international application no. PCT/EP94/02909, filed September 1, 1994. Both of the aforementioned applications are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates to hybrid toxin fragments, and toxins comprising them, derived from *Bacillus thuringiensis* insecticidal crystal proteins.

BACKGROUND OF THE INVENTION

Bacillus thuringiensis (hereinafter B.t.) is capable of producing proteins that accumulate intra-cellularly as crystals. These crystal proteins are toxic to a number of insect larvae. Based on sequence homology and insecticidal specificity, crystal proteins have been categorized into different classes. Best studied are the CryI class of proteins, which are produced as 140 kDa protoxins and are active towards lepidopterans.

To some extent, the mode of action of crystal proteins has been elucidated. After oral uptake, the crystals dissolve in the alkaline environment of the larval midgut. The solubilized proteins are subsequently processed by midgut proteinases to a proteinase-resistant toxic fragment of about 65kDa, which binds to receptors on epithelial cells of the insect midgut and penetrates the cell membrane. This eventually leads to bursting of the cells and death of the larvae.

The activity spectrum of a particular crystal protein is to a large extent determined by the occurrence of receptors on the midgut epithelial cells of susceptible insects. The activity spectrum is co-determined by the efficiency of solubilization of the crystal protein and its proteolytic activation *in vivo*.

The importance of the binding of the crystal protein to midgut epithelial receptors is further demonstrated where insects have developed resistance to one of the crystal proteins, such that the binding of crystal proteins to midgut epithelial cells in resistant insects is significantly reduced.

Toxic fragments of crystal proteins are thought to be composed of three distinct structural domains. Domain I, the most N-terminal domain, consists of 7 α -helices. Domain II comprises 3 β -sheets. Domain III, the most C-terminal domain, folds into a β -sandwich. If projected on CryI sequences, domain I runs from about amino acid residues 28 to 260, domain II from about 260 to 460, and domain III from about 460 to 600.

DESCRIPTION OF THE INVENTION

The present invention concerns hybrid crystal proteins particularly, though not exclusively, involving CryIC together with CryIE, CryIA, or CryIG. The nucleotide sequence of the CryIC gene from B.t. sub. sp. *entomocidus* 60.5 is given in SEQ ID NO:1, and the corresponding amino acid sequence of the protein encoded by said nucleotide sequence is given in SEQ ID NO:2. The nucleotide sequence of the CryIE gene from B.t. sub. sp. *kenyae* 4FI is given in SEQ ID NO:3, and the corresponding amino acid sequence of the protein encoded by said nucleotide sequence is given in SEQ ID NO:4. The nucleotide sequence of a B.t. CryIG gene is given in SEQ ID NO:9, and the corresponding amino acid sequence of the protein encoded by said nucleotide sequence is given in SEQ ID NO:10. These proteins are toxic to lepidopterans, but within this order of insects, each protein has different specificity. CryIC, for example, is particularly active against *S. exigua* and *M. brassicae*.

According to the present invention, there is provided an isolated B.t. hybrid toxin fragment comprising at its C-terminus domain III of a first Cry protein, or a part of said domain or a protein substantially similar to said domain; and comprising at its N-terminus the N-terminal region of a second Cry protein, or a part of said region or a protein substantially similar to said region. For example, a preferred B.t. hybrid toxin fragment according to the present invention comprises at its C-terminus domain III of a first Cry protein and comprises at its N-terminus domains I and II of a second Cry protein. A preferred fragment is one that does not bind to the CryIC binding site in an insect gut when it comprises at its C-terminus domain III of CryIC, or a part of said domain or a protein substantially similar to said domain; or one that does not bind to a CryIA binding site when it comprises at its C-terminus domain III of CryIA, or a part of said domain or a protein substantially similar to said domain.

In the context of the present invention, "substantially similar" means a pure protein having an amino acid sequence that is at least 75% similar to the sequence of a protein according to the invention. It is preferred that the degree of similarity is at least 85%, more preferred that the degree of similarity is at least 90%, and still more preferred that the degree of similarity is at least 95%. In the context of the present invention, two amino acid sequences with at least 75%, 85%, 90%, or 95% similarity to each other have at least 75%, 85%, 90%, or 95% identical or conservatively replaced amino acid residues in a like position when aligned optimally allowing for up to 6 gaps, with the proviso that, with respect to the gaps, a total not more than 15 amino acid residues are affected. For the purpose of the present invention, conservative replacements may be made between amino acids within the following groups:

- (i) Serine and Threonine;
- (ii) Glutamic acid and Aspartic acid;
- (iii) Arginine and Lysine;
- (iv) Asparagine and Glutamine;
- (v) Isoleucine, Leucine, Valine, and Methionine;
- (vi) Phenylalanine, Tyrosine, and Tryptophan; and
- (vii) Alanine and Glycine,

with the proviso that in SEQ ID NO:6, Ser and Tyr are conservative replacements at position 620, and Ala and Glu are conservative replacements at position 618; and that in SEQ ID NO:8, Ser and Tyr are conservative replacements at position 627, and Ala and Glu are conservative replacements at position 625.

In the context of the present invention, "part" of a protein means a peptide comprised by said protein and having at least 80% of the consecutive sequence thereof.

In the context of the present invention, "binding site" means a site on a molecule wherein the binding between site and toxin is reversible such that the K_a between site and toxin is in the order of at least $10^4 \text{ dm}^3 \text{ mole}^{-1}$.

The toxin fragment may comprise at its N-terminus the N-terminal region of any insecticidal protein from B.t. being commonly known as "Cry" or "Cyt", including: CryIA(a),

CryIA(b) CryIA(c), CryIB, CryIC, CryID, CryIE, CryIF, CryIG, CryIH, CryIIA, CryIIB, CryIIC, CryIIIA, CryIIIB, CryIIIB(b), CryIVA, CryIVB, CryIVC, CryIVD, CYTA, CryX1(IIIC), CryX2(IIID), CryX3, CryV, and CryX4, or a part of said region or a protein substantially similar to said region. The toxin fragment may comprise at its C-terminus domain III of CryIC, or a part of said domain or a protein substantially similar to said domain.

Thus, the fragment may comprise domain II of CryIE, CryIB, CryID, CryIA, or CryIG, or a part of said domain II or a protein substantially similar to said domain II, and domain III of CryIC or a part of said domain III or a protein substantially similar to said domain III. It is particularly preferred that the fragment comprises domains I and II of CryIE, CryIB, CryID, CryIA, or CryIG, or a part thereof or a protein substantially similar to said domains I and II, and domain III of CryIC or a part thereof or a protein substantially similar to said domain III.

It is most preferred that the toxin fragment comprises a region at its C-terminus comprising the sequence from amino acid position 454 to position 602 of CryIC, or a sequence substantially similar to said sequence. The fragment may comprise a region at its C-terminus comprising the sequence from amino acid position 478 to 602 of Cry IC, or a sequence substantially similar to said sequence, with the proviso that if the sequence comprising amino acids 478 to 602 of CryIC is fused directly to the C-terminus of domain II of CryIA, CryIB, CryID, CryIE, or CryIG, then the folding of the fusion product is satisfactory to yield an insecticidal component of the fragment. The routineer in the art will recognize that it may be necessary to add a peptide region to the C-terminus of domain II that spaces the C-terminal region of CryIC apart, thus enabling it to fold in such a way as to exhibit insecticidal activity.

It is most particularly preferred that the toxin fragment according to the invention comprises one of the following:

- i) an amino acid sequence from about amino acid 1 to about amino acid 620 in SEQ ID NO:6, or an amino acid sequence from about amino acid 1 to about amino acid 620 in SEQ ID NO:6, wherein with respect to said sequence, at least one of the following alterations is present:

Ile at position 609 is replaced with Leu,

Ala at position 618 is replaced with Glu,

Ser at position 620 is replaced with Tyr;

- ii) an amino acid sequence from about amino acid 1 to about amino acid 627 in SEQ ID NO:8, or an amino acid sequence from about amino acid 1 to about amino acid 627 in SEQ ID NO:8, wherein with respect to said sequence, at least one of the following alterations is present:

Ile at position 616 is replaced with Leu,

Ala at position 625 is replaced with Glu,

Ser at position 627 is replaced with Tyr; and

- iii) an amino acid sequence from about amino acid 1 to about amino acid 602 in SEQ ID NO:12.

Whatever amino acid alterations are permitted, however, one or more of the following residues indicated sequence-wise with respect to the CryIC sequence is invariable: Phe (501), Val (478), Trp (479), and Thr (486).

The invention also includes a hybrid toxin comprising the above disclosed fragment or a toxin at least 85% similar to such a hybrid toxin, which has substantially similar insecticidal activity or receptor binding properties.

The invention still further includes pure proteins that are at least 90% similar to the toxin fragments or hybrid toxins according to the invention.

The invention still further includes recombinant DNA comprising a sequence encoding a protein comprising an amino acid sequence of one of the above-disclosed toxins or fragments thereof. The invention still further includes recombinant DNA comprising the sequence from about nucleotide 1 to about nucleotide 1860 given in SEQ ID NO:5, or DNA similar thereto encoding a substantially similar protein; or recombinant DNA comprising the sequence from about nucleotide 1 to about nucleotide 1881 in SEQ ID NO:7, or DNA similar thereto encoding a substantially similar protein; or recombinant DNA comprising the sequence from about nucleotide 1 to about nucleotide 1806 in SEQ ID NO:11, or DNA similar thereto encoding a substantially similar protein.

In the context of the present invention, "similar DNA" means a test sequence that is capable of hybridizing to the inventive recombinant sequence. When the test and inventive sequences are

double stranded, the nucleic acid constituting the test sequence preferably has a T_m within 20°C of that of the inventive sequence. In the case that the test and inventive sequences are mixed together and denatured simultaneously, the T_m values of the sequences are preferably within 10°C of each other. More preferably, the hybridization is performed under stringent conditions, with either the test or inventive DNA preferably being supported. Thus, either a denatured test or inventive sequence is preferably first bound to a support and hybridization is effected for a specified period of time at a temperature of between 50 and 70°C in double strength citrate buffered saline containing 0.1% SDS, followed by rinsing of the support at the same temperature but with a buffer having a reduced SC concentration. Depending upon the degree of stringency required, and thus the degree of similarity of the sequences, such reduced concentration buffers are typically single strength SC containing 0.1% SDS, half strength SC containing 0.1% SDS and one tenth strength SC containing 0.1% SDS. Sequences having the greatest degree of similarity are those the hybridization of which is least affected by washing in buffers of reduced concentration. It is most preferred that the test and inventive sequences are so similar that the hybridization between them is substantially unaffected by washing or incubation in one tenth strength sodium citrate buffer containing 0.1% SDS. Typical stringent conditions are as follows: hybridization at 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO_4 pH 7.0 , 1 mM EDTA at 50°C ; wash with 2X SSC , 1% SDS, at 50°C .

The recombinant DNA may further encode a protein having herbicide resistance, plant growth-promoting, anti-fungal, anti bacterial, anti-viral, and/or anti-nematode properties. In the case that the DNA is to be introduced into a heterologous organism, it may be modified to remove known mRNA instability motifs (such as AT rich regions) and polyadenylation signals, and/or codons that are preferred by the organism into which the recombinant DNA is to be inserted may be used so that expression of the thus modified DNA in the organism yields substantially similar protein to that obtained by expression of the unmodified recombinant DNA in the organism in which the protein components of the hybrid toxin or toxin fragments are endogenous.

The invention still further includes a DNA sequence complementary to one that hybridizes under stringent conditions with the recombinant DNA according to the invention.

Also included in the present invention are the following: a vector containing such a recombinant (or complementary thereto) DNA sequence; a plant or microorganism that includes and enables expression of such DNA; plants transformed with such DNA; the progeny of such plants that contain the DNA stably incorporated and heritable in a Mendelian manner; and/or the seeds of such plants and such progeny.

The invention still further includes protein derived from expression of the recombinant DNA of the invention, and insecticidal protein produced by expression of the recombinant DNA within plants transformed therewith.

The invention still further includes the following: an insecticidal composition containing one or more of the toxin fragments or toxins comprising them according to the invention; a process for combating insects that comprises exposing them to such fragments or toxins or compositions; and an extraction process for obtaining insecticidal proteins from organic material containing them, comprising submitting the material to maceration and solvent extraction.

DESCRIPTION OF THE FIGURES

Figure 1 shows the generation of hybrid crystal protein genes via *in vivo* recombination. Tandem plasmids (pBD560 and pBD 650) carrying two truncated crystal protein genes in direct repeat orientation are constructed. The 5' located gene (open bar) lacks the protoxin encoding region (solid bar) and of the 3' located gene (dashed bar) part of the domain I encoding region is deleted. *In vivo* recombination between homologous regions (domain II and III) occurs in *recA* + strain JM101. Selection against non-recombinants by digestion with *NotI* and *BamHI* and subsequent transformation results in sets of plasmids encoding hybrid crystal proteins.

Figure 2 shows the alignment of amino acid residues 420 to 630 of CryIE and CryIC. The border between domain II and III is indicated. Only amino acid residues of CryIC that differ from CryIE are depicted; identical residues are indicated by dots. The crossover positions (G27, H13, H7, H8, H17, and H21) in the CryIE/CryIC hybrid toxin fragments according to the invention are indicated on the Figure.

Figure 3 shows the alignment of amino acid residues 420 to 630 of CryIE and CryIC. The border between domain II and III is indicated. Only amino acid residues of CryIC that differ from CryIE are depicted; identical residues are indicated by dots. The crossover positions (F59, F71, F26, and E7) in the CryIC/CryIE hybrid toxin fragments are indicated on the Figure.

Figure 4 shows the results of heterologous competition experiments. Biotinylated CryIC (panel A) and G27 (panel B) are incubated with *S. exigua* BBMV vesicles in the absence (lanes a) or presence of an excess of unlabelled protein as indicated. After the incubation, the vesicles are washed, loaded on a SDS-polyacrylamide gel and blotted to a nitrocellulose membrane. Biotinylated crystal proteins, re-isolated with the vesicles, are visualized using streptavidin-peroxidase conjugate and are indicated on the Figure with an arrow head.

Figure 5 shows the plasmid map of pSB456, which encodes the G27 hybrid toxin fragment and is used to transform the crystal toxin minus strain B.t. 51.

Figure 6A shows the alignment of the *cryIG* and *cryIC* genes with the crossover points of the *cryIG/cryIC* hybrids. The position relative to the first nucleotide of the start codon of *cryIG* is shown.

Figure 6B shows the alignment of the encoded Cry1G and Cry1C proteins with the crossover points of the Cry1G/Cry1C hybrids. The approximate position of the domain II-III border is indicated by #. The position relative to the initiation codon of Cry1G is also indicated.

Figure 7 shows the results of assays measuring the toxicity of Cry1G/Cry1C hybrid toxins towards *Spodoptera exigua*.

DESCRIPTION OF THE SEQUENCES IN THE SEQUENCE LISTING

SEQ ID NO:1 shows the nucleotide sequence of the CryIC gene from B.t. sub. sp. *entomocidus* 60.5.

SEQ ID NO:2 shows the amino acid sequence of the protein encoded by the CryIC gene shown in SEQ ID NO:1.

SEQ ID NO:3 shows the nucleotide sequence of the CryIE gene from B.t. sub. sp. *kenyae* 4FL

SEQ ID NO:4 shows the amino acid sequence of the protein encoded by the CryIE gene shown in SEQ ID NO:3.

5 SEQ ID NO:5 shows the nucleotide sequence encoding a preferred CryIE/CryIC B.t. hybrid toxin fragment according to the invention.

SEQ ID NO:6 shows the amino acid sequence of the protein encoded by the nucleotide sequence shown in SEQ ID NO:5.

SEQ ID NO:7 shows the nucleotide sequence of a CryIA/CryIC hybrid toxin fragment according to the invention.

SEQ ID NO:8 shows the amino acid sequence of the protein encoded by the nucleotide sequence depicted in SEQ ID NO:7.

SEQ ID NO:9 shows the nucleotide sequence of a B.t. CryIG gene.

SEQ ID NO:10 shows the amino acid sequence of the protein encoded by the CryIG gene shown in SEQ ID NO:9.

SEQ ID NO:11 shows the nucleotide sequence encoding a preferred CryIG/CryIC B.t. hybrid toxin fragment (hybrid HK28-24) according to the invention.

SEQ ID NO:12 shows the amino acid sequence of the protein encoded by the nucleotide sequence shown in SEQ ID NO:12.

20 SEQ ID NOs:13-15 are oligonucleotides.

The invention will be further apparent from the following non-limiting Examples, which describe the production of B.t. hybrid toxin fragments according to the invention, taken in conjunction with the associated Figures and Sequence Listing.

EXAMPLES

Production Of Plasmids Encoding Hybrid Toxin Fragments

In the production of plasmids carrying the *CryIC* or *CryIE* genes, *Escherichia coli* XLI-blue (Stratagene Inc.) is used as plasmid host except in cases where JM101 is used as *recA*⁺ background.

5 A vector for the expression of crystal proteins in *E. coli* is derived from pKK233-2 (Pharmacia LKB Biotechnology). The size of pKK233-2 is reduced by deleting an *EcoRI*-*PvuII* fragment carrying the gene encoding tetracycline resistance. Subsequently a 6 bp *XhoI* linker is ligated into the *HindIII* site resulting in pBD10. Plasmid BK⁺ is created by insertion of a *BglIII* linker in the *SacI* site of Bluescript SK⁺ (Stratagene Inc.). The polylinker of BK⁺ from *BglIII* to *XhoI* is
 10 introduced between the *NcoI*-*XhoI* site in pBD10. The resulting expression vector pBD11 contains the highly expressed *trc* promoter, the *lacZ* ribosome binding site and ATG initiation codon. The initiation codon overlaps with a *NcoI* site and is followed by the polylinker to facilitate insertions into the vector. Transcription is terminated by the *rrnB* transcription terminator.

The cloning of the *cryIC* and *cryIE* genes from B.t. sub. sp. *entomocidus* 60.5 and *kenya* 4F1 respectively is as described previously (Honée *et al.*, 1990 (Appl. Environ. Microbiol. 56, pp. 823-825); Visser *et al.*, 1990 (J. Bacteriol. 172, pp. 6783-6788)). For cloning purposes, an *NcoI* site overlapping with the start codon of *cryIC* is created by *in vitro* mutagenesis. A *BglIII* site is created directly downstream of the translation termination codon of *cryIC* by site directed mutagenesis, resulting in the sequence ATAAGATCTGTT (SEQ ID NO:13 - stop-codon
 15 underlined). The *NcoI*-*BglIII* fragment containing the *cryIC* coding region is ligated into pBD11, resulting in *CryIC* expression plasmid pBD150. pBD155 is a derivative of pBD150, in which the polylinker sequences 3' of *cryIC* are deleted.

A *DraI* fragment from pEM14 (Visser *et al.*, 1990) containing the complete *cryIE* gene is cloned in the *EcoRV* site of SK⁺, resulting in plasmid pEM15. Subsequently, an *NcoI* site is
 25 introduced by site directed mutagenesis at the start codon of the gene, and *cryIE* is transferred as an *NcoI*-*XhoI* fragment to pBD11, resulting in *CryIE* expression plasmid pBD160.

Plasmids carrying only toxic fragment-encoding regions of the *cryI* genes are constructed. *Bgl*III linkers are ligated to *Xmn*I sites present at bp position 1835 of *cryIC*, and to the *Hgi*AI site at position 1839 of *cryIE*. Subsequently, *Nco*I-*Bgl*III fragments containing the *cryIC* (1835 bp) and *cryIE* (1839 bp) toxic fragment-encoding regions are ligated into pBD11, resulting in pBD151 and pBD161 respectively as described below.

Tandem plasmids used for the generation of *cryIC-cryIE* hybrid genes are constructed as follows: *Bam*HI linkers are ligated to pBD160 digested with *Hpa*I. This DNA is incubated with *Bam*HI and *Xho*I and the truncated *cryIE* gene running from bp 704 is ligated into pBD151 resulting in pBD560. To construct a tandem plasmid for the generation of *cryIE-cryIC* hybrids, pBD155 is digested with *Nsi*I and *Xho*I. The fragment carrying the truncated *cryIC* gene, running from bp 266, is ligated into *Pst*II/*Xho*I digested pBD161, resulting in plasmid pBD650. Due to polylinker sequences, unique *Not*I and *Bam*HI restriction sites are present between the truncated *cryI* genes present in the tandem plasmids pBD560 and pBD650.

DNA Manipulations And Construction Of Hybrid Toxins

All recombinant DNA techniques are as described by Sambrook *et al.* 1989 (in "Molecular Cloning, A Laboratory Manual: Cold Spring Harbour Press, Cold Spring Harbour). DNA sequencing is performed by the dideoxytriphosphate method with fluorescent dyes attached to the dideoxynucleotides. Analysis is automated by using an Applied Biosystems 370A nucleotide sequence analyzer.

The homology present between *cryI* genes permits intramolecular recombination *in vivo*. Two tandem plasmids are created, each carrying two truncated crystal protein genes overlapping only in domains II and III. Therefore, recombination occurs only in regions encoding domains II and III. In-frame recombinations, which can be selected for by restriction enzyme digestion, generate plasmids that express full size 140 kDa hybrid protoxins. To generate *in vivo* recombinants, a tandem plasmid (either pBD560 or pBD650; Figure 2) is transferred to JM101. 5 mg of DNA is isolated from independently generated recombinants and is digested with *Not*I and *Bam*HI cutting between the two truncated *cryI* genes to select against non-recombinants, and the

DNA is transformed to *E. coli* XL1-blue. 5 single colonies are grown and protein patterns and plasmid content are analyzed.

CryIC/CryIE and CryIE/CryIC hybrid toxins are generated using the tandem plasmids pBD560 and pBD650 respectively, which are allowed to recombine in a *recA*⁺ background. DNA is isolated, digested, and transferred to *recA*⁻ strain as described above.

100 colonies of 20 independent experiments are analyzed on SDS-PAGE. 85% of these clones produce a 140 kDa protein indicating in frame recombinations between *cryIC* and *cryIE*, and *cryIE* and *cryIC*, respectively. In *E. coli*, CryI proteins are produced as crystals that can be solubilized *in vitro* at high pH. Approximately 15% of hybrid toxins produced as above are solubilized at high pH. The recombinants producing soluble hybrid toxins are first classified using restriction enzymes. Subsequently, for each class, the crossover point of selected hybrids is determined by DNA sequence analysis. All crossovers resulting in soluble hybrid toxins occur in or very close to domain III.

Protein Purification And Analysis

Crystal proteins are isolated essentially as described by Convents *et al.* (J. Biol. Chem. 265, pp. 1369-1375; Eur. J. Biochem., 195, pp. 631-635). Briefly, recombinant *E. coli* are grown at 30°C in 250 ml TB medium to an OD₆₆₀ of 10-15. Crystals isolated from the *E. coli* lysate are solubilized during incubation for 2 hours in 20mM Na₂CO₃, 10 mM dithiothreitol, 100 mM NaCl, pH10, at 37°C. The pH of the solution is lowered to 8 with Tris-HCl and incubated with trypsin. The toxin solution is dialysed against 20 mM Tris-HCl, 100 mM, NaCl pH9. Subsequently, the toxic fragment is purified on a Mono Q 5/5 column connected to a fast-protein liquid chromatography (FPLC) system (Pharmacia LKB Biotechnology). Proteins are separated by 7.5% sodium dodecyl sulfate-polyacrylamide gel electrophoreses.

Biochemical Analysis And Isolation Of 65 kDa Toxic Fragments

Isolated crystals of purified CryIC, CryIE, and the hybrid proteins are solubilized at high pH and incubated with trypsin. Like CryIC and CryIE, all soluble hybrid toxins with crossovers in domain III are converted to stable 65 kDa fragments. The 65 kDa fragments can be purified using

anion exchange chromatography under similar conditions as the parental proteins. Hybrids F59 and F71, which have crossovers in domain II, are completely degraded by trypsin. Apparently, although these hybrids do not precipitate as insoluble aggregates, trypsin cleavage sites buried in the parental proteins may become exposed to trypsin. Because of this phenomenon, no 65 kDa fragments are isolated from F59 and F71.

Table 1 shows the constitution of 5 CryIE/CryIC hybrid toxins: (G27, H8, H17, H13, H7, and H21) and 4 CryIC/CryIE hybrid toxins (F59, F71, F26, and E7) with reference to the CryIC and CryIE proteins from which they are derived. The amino acid sequences of the CryIE/CryIC toxins comprising the toxic fragments of the present invention run to amino acid 1189 of the CryIC parent protein. The amino acid sequences of the CryIC/CryIE hybrid toxins run to amino acid 1171 of the CryIE parent protein. Table 1 also shows the relative insecticidal effectiveness of these various hybrid toxins with respect to the CryIC and CryIE proteins.

TABLE 1

| Toxin | aa IE | aa IC | <i>M. sexta</i> | <i>S. exigua</i> | <i>M. brassicae</i> |
|-------|----------------|---------|-----------------|------------------|---------------------|
| IC | 0 | 28-627 | ++ | ++ | ++ |
| IE | 29-612 | 0 | ++ | - | - |
| | | | | | |
| G27 | 1-474 | 478-627 | ++ | ++(+) | +(+) |
| H8 | 1-497 | 501-627 | ++ | - | - |
| H17 | 1-529 | 533-627 | ++ | - | - |
| H7 | 1-577 | 588-627 | - | - | - |
| H21 | 1-605 | 621-627 | | | |
| | | | | | |
| F59 | 421-612 | 1-423 | - | - | - |
| F71 | 428-612 | 1-430 | - | - | - |
| F26 | 455-612 (1171) | 1-458 | ++ | - | - |
| E7 | 588-612 (1171) | 1-602 | ++ | ++ | ++ |

Table 1. Constitution and toxicity of hybrid toxins with respect to the parent proteins. Most bioassays were performed with purified toxin fragments. In case of CryIC these run from about aa 28 to about aa 627, and in case of CryIE till 612. The length of complete protoxins is indicated between brackets.

5

Insect Toxicity Assays And Insecticidal Activity of *cryIC/cryIE* Hybrid Gene Products

Bacterial cultures are concentrated to OD₆₆₀ 6.0, and 100 ml are spotted on 2 cm² of artificial diet in a 24-well tissue culture plate. Alternatively, diluted samples of purified toxins are applied to the diet. Second instar larvae of either *S. exigua*, *M. brassicae*, or *M. sexta* are fed on this diet (16 per sample dilution) for 5 days, after which the larval weight is scored. The relative growth (EC50, the concentration giving 50% growth reduction) is determined by calculating the ratio between the mean weight of larvae grown on diet supplemented with toxin and the mean weight of control larvae grown on a diet without toxin. *M. sexta* egg layers are supplied by Carolina Biological Supply Company, North Carolina, USA.

The toxic fragments encoded by the hybrid gene products are tested for activity towards three different insect species as described above. *M. sexta* is susceptible to both CryIC and CryIE. As may be anticipated from their sensitivity to trypsin, hybrids F59 and F71 are not active against this insect (Table 1). Although H7 is converted by trypsin to stable 65 kDa proteins, it is not toxic to *M. sexta*. All of the other hybrids given in Table 1 are toxic and are apparently in the native, biologically active conformation.

The 65 kDa fragment of CryIC is highly toxic towards *S. exigua* and *M. brassicae*, whereas CryIE is not. G27 (Table 1; Figure 2), a CryIE-CryIC hybrid with a crossover at the junction of domain II and III is active towards both insects. This demonstrates that domain III of CryIC confers full activity towards *S. exigua* and *M. brassicae*. Hybrid H8, which differs in only three amino acid residues (see Figure 3) from G27, although active against *M. sexta*, is not active against *S. exigua* and *M. brassicae*.

F26 (Table 1; Figure 3), the reciprocal hybrid of G27, in which domain III of CryIC has been exchanged by domain III of CryIE, is not active against *S. exigua* or *M. brassicae*. Apparently, although the protein is toxic to *M. sexta*, the CryIC sequences running from amino acid

28-462 are not sufficient to kill *S. exigua* and *M. brassicae*. Only when CryIC sequences up to amino acid residue 602 are present in the hybrid (E7) is insecticidal activity against these insects restored.

The present disclosure indicates that amino acid residues from 478-602 of CryIC can confer high insecticidal activity to CryIE against *S. exigua* and *M. brassicae*.

Biotinylation Of Crystal Proteins And Binding Assays

Biotinylation is performed using biotin-N-hydroxysuccinimide ester essentially as described by the manufacturer (Amersham). 1 mg of crystal protein is incubated with 40 ml biotinylation reagent in 50 mM NaHCO₃, 150 mM NaCl, pH8, for one hour at 20°C. The solution is loaded on a Sephadex 25 column equilibrated with the same buffer containing 0.1% BSA to remove unbound biotin, and samples of the fractions are spotted on a nitrocellulose membrane. Fractions containing biotinylated crystal proteins are visualized using streptavidine-peroxidase conjugate (Amersham) which catalyzes the oxidation of luminol, resulting in chemiluminescence (ECL, Amersham), and pooled.

Brush border membrane vesicles are isolated as described by Wolfersberger *et al.* (1987) (Comp. Biochem. Physiol. 86a, pp. 301-308) except that the vesicles are washed once more with isolation buffer containing 0.1% Tween 20. Binding of biotinylated crystal proteins to brush border membrane vesicles (100 mg/ml) is performed in 100 ml of PBS containing 1% BSA, 0.1% Tween-20 (pH 7.6). Vesicles (20 µg vesicle protein) are incubated with 10 ng biotinylated crystal proteins in the presence or absence of 1000-fold excess of unlabelled crystal proteins for 1 hour at 20°C. Subsequently, the vesicles are re-isolated by centrifugation for 10 minutes at 14,000 g in an Eppendorf centrifuge, washed twice with binding buffer, re-suspended in sample buffer, denatured by heating, and loaded on 7.5% polyacrylamide gels. After electrophoresis, proteins are blotted to nitrocellulose membranes and biotinylated crystal proteins that are re-isolated with the vesicles are visualized by incubation of the nitrocellulose with streptavidin-peroxidase conjugate (Amersham), which catalyzes the oxidation of luminol, resulting in chemiluminescence (ECL, Amersham).

Because binding to epithelial gut cells is a key step in the mode of action of crystal proteins, the binding of crystal proteins to *S. exigua* brush border membrane vesicles is investigated in heterologous competition experiments. Competition experiments demonstrate that the binding of labeled CryIC (Figure 4A, lane a) and labeled F26 (not shown) can be outcompeted by an excess of both unlabelled CryIC (lane b) or F26 (lane e) but not with an excess of G27 (lane c) or CryIE (lane d). Furthermore, binding of labeled G27 (Figure 4B, lane a) and labeled CryIE (not shown) can be outcompeted by an excess of G27 (lane b) or CryIE (lane d), but not with an excess of CryIC (lane a) or F26 (lane e). From these results, it is concluded that G27 and CryIE recognize the same binding sites on *S. exigua* midgut membranes and that these sites differ from those that are recognized by CryIC and F26. The toxicity and binding assays combined demonstrate that G27 is as toxic as CryIC but that it binds a receptor different therefrom. As insects can develop resistance against a crystal protein by changing receptor binding characteristics, G27 may be used in resistance management programs as an alternative to CryIC.

Expression of *cryIE/cryIC* Hybrid Toxin Genes In Heterologous Systems

The G27 *cryIE/cryIC* hybrid toxin gene is expressed in *E. coli*, and the gene product exhibits at least the same insecticidal activity (at least against *Spodoptera*) as CryIC. Moreover, the product exhibits an increase in such activity when expressed in a *Bacillus thuringiensis* strain (see below). The gene encoding the G27 hybrid toxin is introduced into a suitable shuttle vector system, which is then introduced into an appropriate B.t. host. Such transformed cells are then cultured, and the resulting toxin from both whole cultures and purified crystals is assayed for insecticidal activity.

Construction Of A G27-Containing Shuttle Vector, Transformation Of Bt51, And Purification Of Toxin Protein Therefrom

The gene encoding hybrid G27 (3.4 kb) is cleaved from a pKK233 *E. coli* expression plasmid using *NcoI* and *XhoI*. The *XhoI* site is filled in using the Klenow fragment of *E. coli* DNA Polymerase I. The resulting fragment is ligated to *NcoI/SmaI*-digested pSB635 (pBluescriptKS+, P_{cryIC} , and the CryIA(c) transcription terminator). The resulting plasmid, pSB453, is digested with *Apal* and *NotI*, yielding a 4.2 kbp fragment carrying the promoter, the hybrid G27 ORF, and the terminator. This fragment is ligated to *Apal/NotI*-digested pSB634 (shuttle vector containing

pBC16.1 and pBluescriptKS+), yielding pSB456 (see Figure 5). Plasmid DNA isolated from *E. coli* DH10B is used to transform the crystal toxin minus B.t. strain, Bt51. Positive isolates are tetracycline resistant, show the presence of pSB456, and contain large inclusions corresponding to a 135 kDa protein (as determined by SDS-PAGE). G27 hybrid toxin samples are prepared from cultures of transformed Bt51 grown through sporulation at 30°C in CYS-Tc¹⁰ media. Insecticidal bioassays (Table 2) are performed on both full whole cultures and on washed crystal protein preparations. Controls include Bt51 (pSB440) containing the CryIC toxin and Bt51 (pSB636) containing CryIE. Toxin concentrations are estimated by SDS-PAGE.

TABLE 2

| Toxin | LC ₅₀ | | | | |
|----------------|---------------------|-------|------------------------------|---------|--------|
| | Whole Culture (ppt) | | Washed Crystal Protein (ppm) | | |
| CryIC | 56(2) | 36(2) | 40(4) | 7.8(2) | 8.1(4) |
| CryIE | 79(1) | 78(1) | 33(4) | 11.1(6) | 7.5(4) |
| G27 | 29(2) | 21(2) | 25(4) | 4.7(4) | 6.0(4) |
| Ratio (IC/G27) | 1.93 | 1.71 | 1.60 | 1.66 | 1.35 |

Table 2. Bioassay of the hybrid toxin G27 in comparison to CryIC and CryIE. The number of samples is given in parentheses. The hybrid toxin G27 is about 50% more effective than either CryIE or CryIC with respect to toxicity to *Spodoptera* sp.

Production And Selection Of Cry1G/Cry1C Hybrid Toxins

To obtain Cry1G/Cry1C hybrid toxins by *in vivo* recombination, expression vector pHK26 was constructed with a C-terminal truncated *cryIG* (a.k.a. Cry9A) gene (see, SEQ ID NO:9) and a N-terminal truncated *cryIC* gene (see, SEQ ID NO:1) cloned in tandem. The plasmid pHK26 contains the *trc* promoter followed by bases 1-1650 of *cryIG*, part of the pBluescript SK+ polylinker, and bases 266-3570 of *cryIC*. pHK26 is a derivative of pRM7 in which the *cry1A(b)* coding sequences from *NcoI* to *BglIII* have been replaced by part of the *cryIG* gene. The 1650 bp *NcoI-BglIII* *cryIG* fragment was isolated by PCR amplification from plasmid pSB1501 using the primers dGCTAGCCATGGATCAAAATAAACACGGAATTATTG (SEQ ID NO:14) and dCTGGTCAGATCTTTGAAGTAGAGCTCC (SEQ ID NO:15). After allowing

intramolecular recombination of pHK26 in *E. coli* strain JM101, plasmid DNA was isolated and digested with *Bam*HI and *Pin*AI to linearize non-recombinant plasmids. Both *Bam*HI as well as *Pin*AI have unique recognition sites in pHK26, in the polylinker and at position 1074 of *cry*IC, respectively. The overlap between the two truncated *cry* genes in pHK26 that allows recombination extends approximately 1400 base pairs, yet primary interest was in recombinations in or close to domain III. Therefore, *Pin*AI was chosen rather than a second enzyme with a recognition site in the polylinker. This strategy allowed linearization of recombinants with crossovers in front of the *Pin*AI site, thereby effectively selecting for recombinants with crossovers in or near the domain III-encoding sequences.

Digested plasmids were transferred to *E. coli* XL1 cells by transformation, and plasmids from transformants were subsequently analyzed by restriction enzyme digestion and DNA electrophoresis. Over 80% of the transformants contained a plasmid with an insert size corresponding to a single, intact *cry* gene, indicating that selection for homologous recombination events had been efficient. Thirty separate colonies were grown in TB medium and assayed for production of alkaline-soluble protoxins that could be converted to stable 65 kD toxic fragments upon trypsin incubation. This screening method yielded 6 colonies producing a stable 65 kD toxic fragment of the expected size. The location of the crossovers in the hybrid genes was first determined by restriction analysis and finally by nucleotide sequencing. Only three different crossover sites occurred in the 6 hybrid genes thus tested. The hybrid genes were designated HK28-12, HK28-1, and HK28-24. The location of the three different crossover sites is shown in Figures 6A and 6B. The three crossovers are located close to the border between domains II and III, with the three hybrid toxins, designated HK28-12, HK28-1, and HK28-24, differing only one amino acid from each other. Both the solubility of the hybrid protoxins as well as the occurrence of trypsin-resistant products of the expected size suggested that these hybrids proteins were properly folded and might have biological activity. This was subsequently tested against larvae of *Spodoptera exigua*.

Toxicity of CryIG/CryIC Hybrid Toxins Towards *Spodoptera exigua*

The *cryIC*, *cryIG*, and newly isolated *cryIG/cryIC* hybrid genes were introduced in *E. coli* strain XL1-blue and grown for 48 hours at 28°C in TB medium with ampicillin. Cells were disrupted by sonification, and protoxin-containing crystals were isolated by centrifugation. After washing the crystals, the protoxins were solubilized at high pH and the concentration of the 140 kD protoxins in the supernatant was estimated by SDS-PAGE. These samples were assayed for their toxicity to *S. exigua* larvae. Results are shown in Figure 7.

CryIG protoxin is much less toxic to *S. exigua* than CryIC. The hybrids containing domain III of CryIC are significantly more toxic than CryIG. These results show that, as was demonstrated earlier for CryIE and CryIA(b), CryIG can be made considerably more toxic to *S. exigua* by substituting its domain III with that of CryIC. For example, hybrid HK28-24 (SEQ ID NO:12) is much more toxic to *S. exigua* than CryIG (SEQ ID NO:10). Hybrid HK28-24 is also much more toxic to *S. frugiperda* than CryIG (data not shown).

Although the present invention has been particularly described with reference to the production of CryIE/CryIC and CryIG/CryIC hybrid toxins, the routineer in the art will appreciate that many other hybrid toxins having improved insecticidal characteristics may be produced according to the present disclosure. SEQ ID NOs:7 and 8, for example, depict the nucleotide and amino acid sequences, respectively, of a CryIA/CryIC hybrid toxin fragment according to the invention that has improved insecticidal activity. Hybrid toxins may be produced comprising domain III of CryIC and the N-terminal region, including domains I and II, of any other Cry protein. In terms of bioassays, the hybrid toxin-carrying transformants may be grown in SOP media to expedite the assay procedures and reduce the volumes of material required. Moreover, the genes encoding the CryIE/CryIC, CryIG/CryIC, CryIA/CryIC, and/or other hybrid toxins according to the invention may be transferred into toxin-encoding strains of B.t. and/or integrated into the chromosome of selected strains of B.t. or introduced into plant genomes to provide for insecticidal activity *in situ* within the plant *per se*. In this regard, it is particularly preferred that the recombinant DNA encoding the toxins is modified so that codons that are preferred by the plant into which the recombinant DNA is to be inserted are used, whereby expression of the thus

modified DNA in the plant yields substantially similar protein to that obtained by expression of the unmodified recombinant DNA in the organism in which the protein components of the hybrid toxin or toxin fragments are endogenous.

Isolation of Additional B.t. Toxin Genes Based on Sequence Similarity to Known B.t. Toxin Genes

A library is plated at a density of approximately 8,000 pfu per 10 cm Petri dish, and filter lifts of the plaques are made after 7 hours growth at 37°C. The plaque lifts are probed with the cDNA set forth in SEQ ID NO:1, 3, or 9 labeled with 32P-dCTP by the random priming method by means of a PrimeTime kit (International Biotechnologies, Inc., New Haven, CT). Exemplary hybridization conditions are 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄ pH 7.0, 1 mM EDTA at 50°C. After hybridization overnight, the filters are washed with 2X SSC, 1% SDS at 50°C. Positively hybridizing plaques are detected by autoradiography. After purification to single plaques, cDNA inserts are isolated, and their sequences determined by the chain termination method using dideoxy terminators labeled with fluorescent dyes (Applied Biosystems, Inc., Foster City, CA). This experimental protocol can be used by one of ordinary skill in the art to obtain B.t. toxin genes substantially similar to those set forth in the Sequence Listing.

What Is Claimed Is:

1. An isolated *Bacillus thuringiensis* hybrid toxin fragment, comprising:
 - a) at a C-terminus of said fragment, domain III of a first Cry protein; and
 - b) at an N-terminus of said fragment, an N-terminal region of a second Cry protein.
2. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, wherein said first Cry protein is CryIC.
3. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, wherein said second Cry protein is selected from the group consisting of CryIA, CryIE, and CryIG.
4. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 3, wherein said second Cry protein is CryIA.
5. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 3, wherein said second Cry protein is CryIE.
6. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 3, wherein said second Cry protein is CryIG.
7. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, wherein said first Cry protein is CryIC, and wherein said second Cry protein is CryIA, CryIE, or CryIG.
8. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, wherein said N-terminal region of said second Cry protein comprises domain II of said second Cry protein.
9. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, wherein said N-terminal region of said second Cry protein comprises domains I and II of said second Cry protein.
10. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, wherein said C-terminus comprises the sequence from amino acid position 454 to position 602 of Cry IC, or a

sequence substantially similar to said sequence from amino acid position 454 to position 602 of Cry IC.

11. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 10, wherein said C-terminus comprises the sequence from amino acid position 454 to position 602 of SEQ ID NO:2, or a sequence substantially similar to said sequence from amino acid position 454 to position 602 of SEQ ID NO:2.

12. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, wherein said C-terminus comprises the sequence from amino acid position 478 to 602 of Cry IC, or a sequence substantially similar to said sequence from amino acid position 478 to 602 of Cry IC.

13. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 12, wherein said C-terminus comprises the sequence from amino acid position 478 to position 602 of SEQ ID NO:2, or a sequence substantially similar to said sequence from amino acid position 478 to position 602 of SEQ ID NO:2.

14. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, comprising a sequence selected from the group consisting of:

- a) amino acids 1-620 of SEQ ID NO:6;
- b) amino acids 1-620 of SEQ ID NO:6, wherein at least one of the following substitutions is present:
 - Ile at position 609 is replaced with Leu,
 - Ala at position 618 is replaced with Glu,
 - Ser at position 620 is replaced with Tyr; and
- c) a sequence substantially similar to amino acids 1-620 of SEQ ID NO:6.

15. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, comprising a sequence selected from the group consisting of:

- a) amino acids 1-627 of SEQ ID NO:8;
- b) amino acids 1-627 of SEQ ID NO:8, wherein at least one of the following substitutions is present:

Ile at position 617 is replaced with Leu,
 Ala at position 625 is replaced with Glu,
 Ser at position 627 is replaced with Tyr; and

- c) a sequence substantially similar to amino acids 1-627 of SEQ ID NO:8.

16. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, comprising a sequence selected from the group consisting of:

- a) amino acids 1-602 of SEQ ID NO:12; and
 b) a sequence substantially similar to amino acids 1-602 of SEQ ID NO:12.

17. An isolated DNA molecule encoding a protein that comprises the amino acid sequence of the hybrid toxin fragment of claim 1.

18. An isolated DNA molecule encoding a protein that comprises the amino acid sequence of the hybrid toxin fragment of claim 14.

19. An isolated DNA molecule encoding a protein that comprises the amino acid sequence of the hybrid toxin fragment of claim 15.

20. An isolated DNA molecule encoding a protein that comprises the amino acid sequence of the hybrid toxin fragment of claim 16.

21. An isolated *Bacillus thuringiensis* hybrid toxin fragment according to claim 1, wherein said hybrid toxin fragment binds to a binding site in an insect gut that is different than the site bound by said first Cry protein.

22. An isolated DNA molecule according to claim 17, which further encodes a protein having at least one of the following properties: herbicide resistance, plant growth-promoting, anti-fungal, anti-bacterial, anti-viral, and anti-nematode properties.

23. An isolated DNA molecule according to claim 17, which is modified to optimize expression in a heterologous host, said modifications selected from the group consisting of codon optimization for the intended host and removal of known mRNA instability motifs or polyadenylation signals.

24. An isolated DNA molecule that is complementary to the DNA molecule of claim 17.
25. A recombinant vector comprising the DNA molecule of claim 17.
26. An isolated cell transformed with the DNA molecule of claim 17.
27. A plant transformed with the DNA molecule of claim 17, wherein the progeny of such plant contains the DNA molecule stably incorporated and heritable in a Mendelian manner.
28. Seeds of the plant of claim 27.
29. Protein derived from expression of the DNA molecule of claim 17.
30. An insecticidal composition comprising the hybrid toxin fragment of claim 1.
31. A process for controlling insects, comprising exposing them to the insecticidal composition of claim 30.
32. A method of producing a protein, comprising expressing the DNA molecule of claim 17.
33. An insecticidal composition comprising the isolated cell of claim 26.
34. A process for controlling insects, comprising exposing them to the insecticidal composition of claim 33.
35. An isolated *Bacillus thuringiensis* hybrid toxin fragment, comprising amino acids 1-602 of SEQ ID NO:12.
36. An isolated *Bacillus thuringiensis* hybrid toxin fragment that has at least 95% sequence identity with, and has substantially the same insecticidal specificity and substantially the same insecticidal activity as the hybrid toxin fragment of claim 35.
37. An isolated DNA molecule encoding a protein that comprises the sequence of the hybrid toxin fragment of claim 35.

38. An isolated DNA molecule encoding a protein that comprises the sequence of the hybrid toxin fragment of claim 36.
39. An isolated DNA molecule that comprises the sequence of nucleotides 1-1806 of SEQ ID NO:11.
40. An isolated DNA molecule that hybridizes to the DNA molecule of claim 39 under the following set of conditions: hybridization at 7% sodium dodecyl sulfate (SDS), 0.5 M NaPO₄ pH 7.0, 1 mM EDTA at 50°C; wash with 2X SSC, 1% SDS, at 50°C.

ABSTRACT

The present invention provides, *inter alia*, a B.t. hybrid toxin fragment comprising at its C-terminus domain III of a first Cry protein, or a part of said domain or a protein substantially similar to said domain; and comprising at its N-terminus the N-terminal region of a second Cry protein, or
5 a part of said region or a protein substantially similar to said region.

FIG. 1

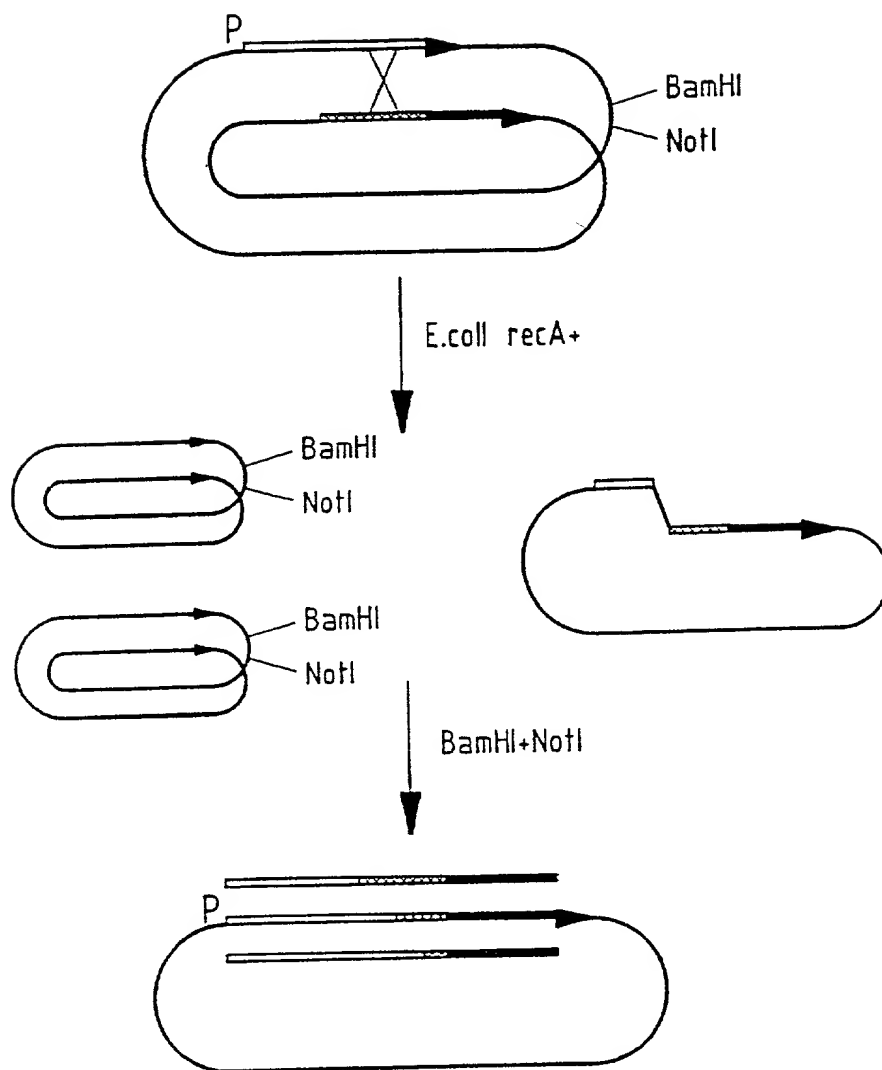


FIG. 2

CryE-CryIC HYBRIDS

CrYIE (420) *vgtsr-lshutlts-lvntnltslptfwrh* HSATNTNTINPDIITQIPLUKGFRLLGGCTS
 CrYIC (423) *e.....c.a.fuqrsqtpfl.tgvv.s...* R...L...D.E.R.N.....UW....
 Domain II ← → III G27 ↓

CPYIE (525) SRDARITUAIG-----GQIRUDMTLEKTMEIGESLTSRFSYVNESNPFSEFRANPDIIIRIA
CPYIC (528)UI.LI.AASTIGUG..US.N.P.Q.....N.....R.D.....G.S

H8 H17
↑ ↓
VIKGPGTGDILRRNTIGEFSLQNINSPITORVRLRFRYAS/
. . . T . . . F . D . . .

H21
↓
EELP-----IRGGELYIDKIELILADATFEEEYDLEAQQ (615)
QPLFGAGS.SS-----I-----A.S----- (630)

 = β sheet = loop III

FIG. 4

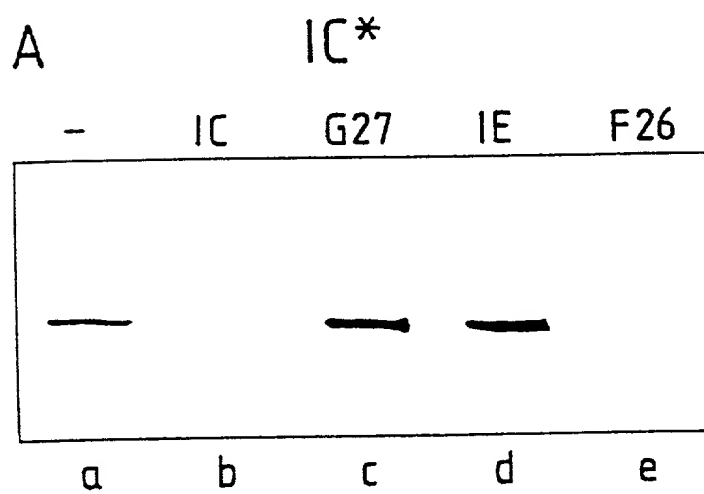
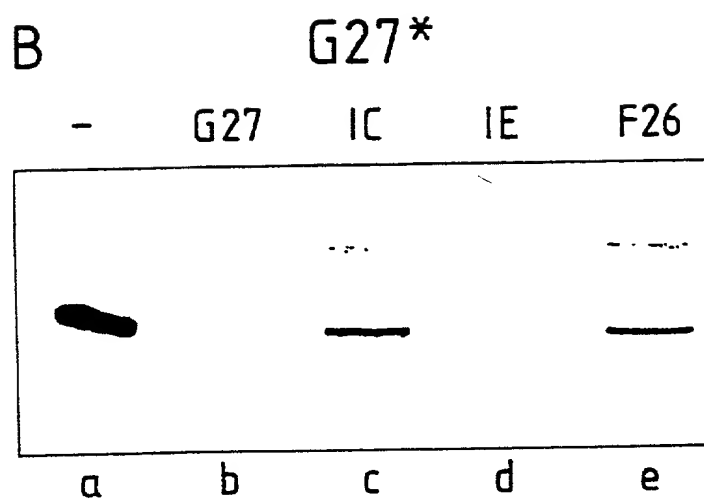
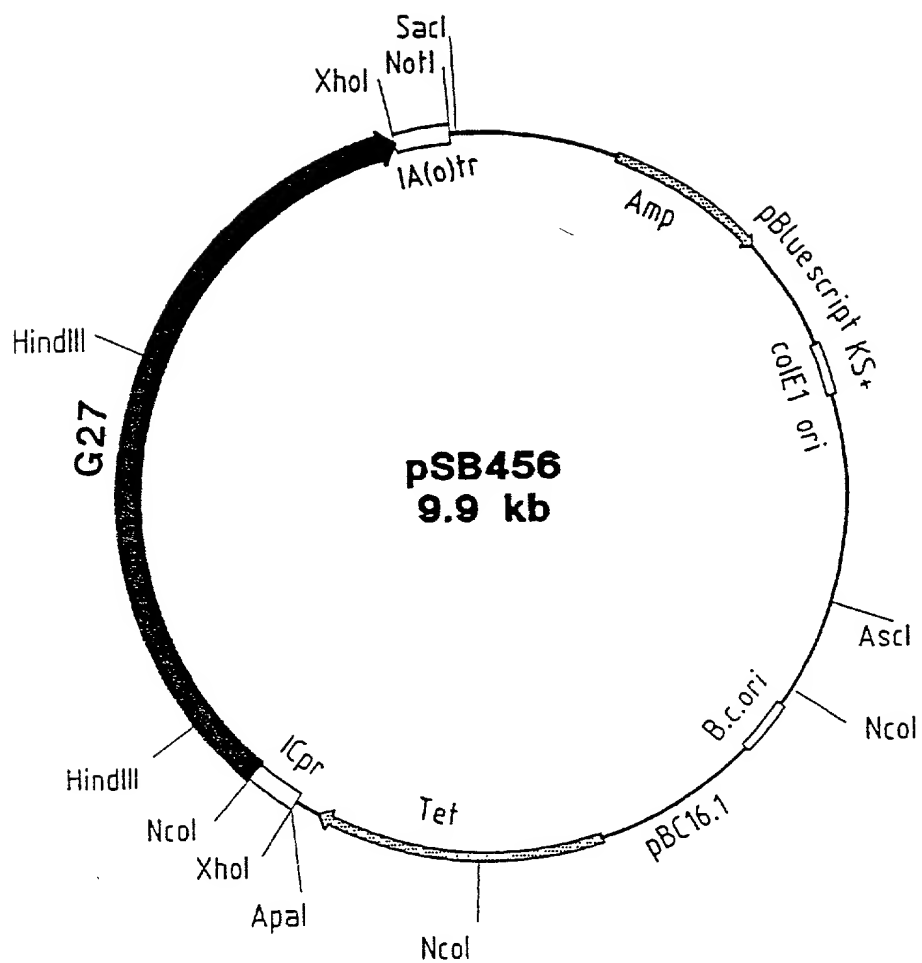


FIG. 5



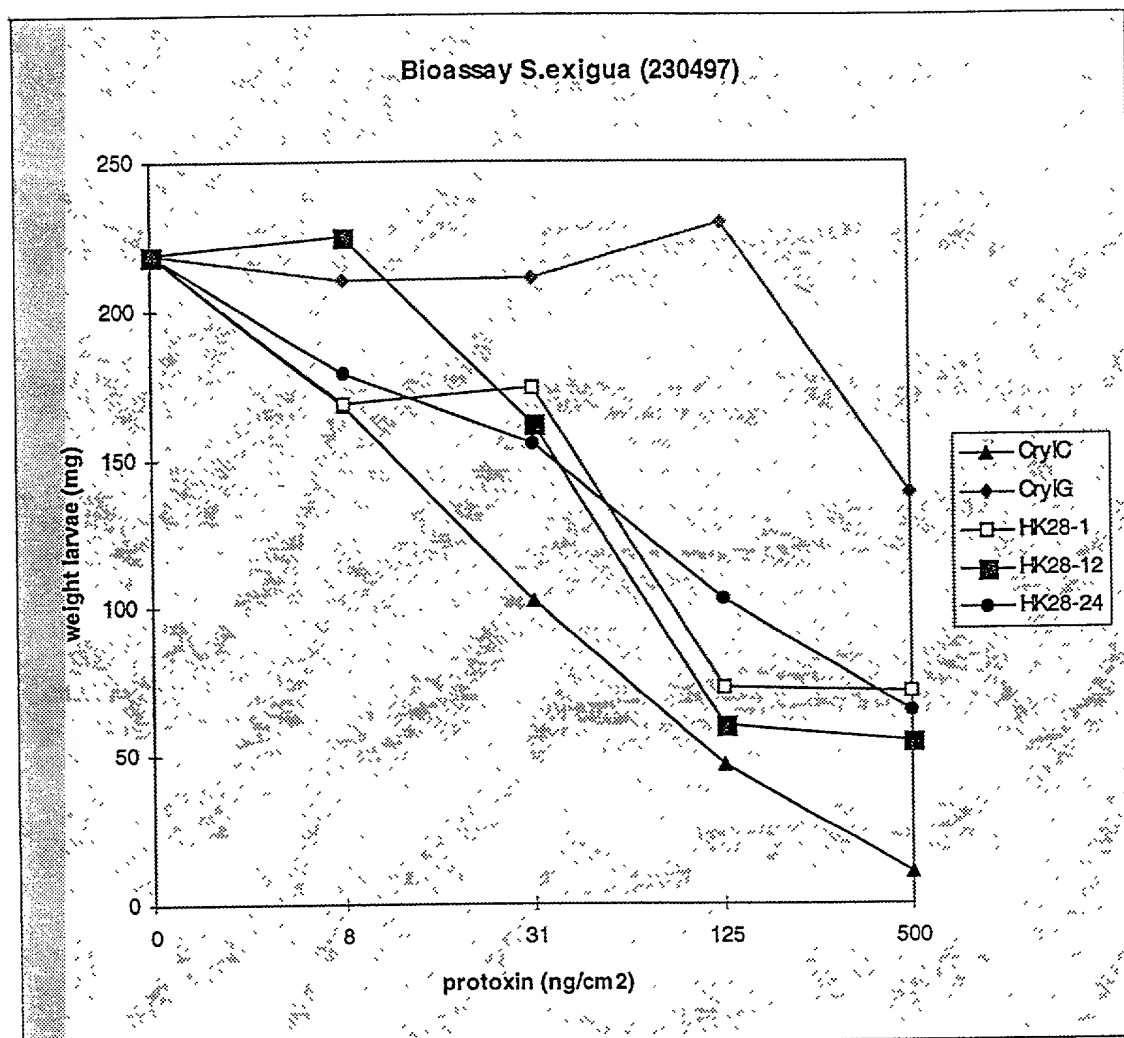
[illegible]

Hybrid HK28-

[illegible]

Hybrid HK28-

FIG. 7



DECLARATION AND POWER OF ATTORNEY FOR U.S. PATENT APPLICATIONS

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,
and

I believe I am an original, first and joint inventor of the subject matter which is claimed
and for which a patent is sought on the invention entitled

Hybrid Toxin

the specification of which was filed on December 31, 1997 as U.S. Application No. 09/001,982.

I hereby state that I have reviewed and understand the contents of the above identified
specification, including the claims.

I acknowledge my duty to disclose all information which is known by me to be material to
the patentability of this application as defined in 37 C.F.R. §1.56.

I hereby claim the benefit under 35 U.S.C. §119(a)-(d) or §365(b) of any foreign
application(s) for patent or inventor's certificate listed below and under 35 U.S.C. §365(a) of any
PCT international application(s) designating at least one country other than the United States
listed below and have also listed below any foreign application(s) for patent or inventor's
certificate or any PCT international application(s) designating at least one country other than
the United States for the same subject matter and having a filing date before that of the
application the priority of which is claimed for that subject matter:

| <u>Country, Region or PCT</u> | <u>Application No.</u> | <u>Filing Date</u> | <u>Priority Claimed</u> |
|-----------------------------------|------------------------|--------------------|-----------------------------|
| Great Britain | 9318207.9 | September 2, 1993 | Yes |

I hereby claim the benefit under 35 USC §119(e) of any United States provisional
application(s) listed below:

None

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) listed below and under 35 U.S.C. §365(c) of any PCT international application(s) designating the United States listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in said prior application(s) in the manner required by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose all information known by me to be material to patentability as defined in 37 C.F.R. §1.56 which became available between the filing date(s) of the prior application(s) and the national or PCT international filing date of this application:

| <u>United States Application No.</u> | <u>United States Filing or §371 Date</u> | <u>Status or U.S. Patent No.</u> | <u>International Application No.</u> | <u>International Filing Date</u> |
|--|--|--------------------------------------|--|--------------------------------------|
| 08/602,737 | February 21, 1996 | Pending | PCT/EP94/02909 | September 1, 1994 |

I hereby appoint the attorneys and agents associated with Customer No. 001095, respectively and individually, as my attorneys and agents, with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.


Please address all communications to J. Timothy Meigs, Novartis Corporation, Patent and Trademark Dept., P.O. Box 12257, Research Triangle Park, NC 27709-2257.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FIRST JOINT INVENTOR:

Full name : **Hendrik Jan Bosch**

Signature :



Date :

04/09/98
(MM/DD/YY)

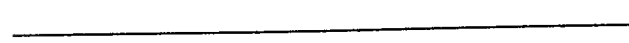
Citizenship : Netherlands

Residence : Oortlaan 20
NL-3572 ZM Utrecht
The Netherlands

SECOND JOINT INVENTOR:

Full name : **Willem Johannes Stiekema**

Signature :



Date :

(MM/DD/YY)

Citizenship : Netherlands

Residence : Leonard Roggeveenstraat 21
NL-6708 SL Wageningen
The Netherlands

IMPORTANT: Before this declaration is signed, the patent application (the specification, the claims and this declaration) must be read and understood by each person signing it, and no changes may be made in the application after this declaration has been signed.

DECLARATION AND POWER OF ATTORNEY FOR U.S. PATENT APPLICATIONS

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,
and

I believe I am an original, first and joint inventor of the subject matter which is claimed
and for which a patent is sought on the invention entitled

Hybrid Toxin

the specification of which was filed on December 31, 1997 as U.S. Application No. 09/001,982.

I hereby state that I have reviewed and understand the contents of the above identified
specification, including the claims.

I acknowledge my duty to disclose all information which is known by me to be material to
the patentability of this application as defined in 37 C.F.R. §1.56.

I hereby claim the benefit under 35 U.S.C. §119(a)-(d) or §365(b) of any foreign
application(s) for patent or inventor's certificate listed below and under 35 U.S.C. §365(a) of any
PCT international application(s) designating at least one country other than the United States
listed below and have also listed below any foreign application(s) for patent or inventor's
certificate or any PCT international application(s) designating at least one country other than
the United States for the same subject matter and having a filing date before that of the
application the priority of which is claimed for that subject matter:

| <u>Country, Region or PCT</u> | <u>Application No.</u> | <u>Filing Date</u> | <u>Priority Claimed</u> |
|-----------------------------------|------------------------|--------------------|-----------------------------|
| Great Britain | 9318207.9 | September 2, 1993 | Yes |

I hereby claim the benefit under 35 USC §119(e) of any United States provisional
application(s) listed below:

None

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) listed below and under 35 U.S.C. §365(c) of any PCT international application(s) designating the United States listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in said prior application(s) in the manner required by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose all information known by me to be material to patentability as defined in 37 C.F.R. §1.56 which became available between the filing date(s) of the prior application(s) and the national or PCT international filing date of this application:

| <u>United States Application No.</u> | <u>United States Filing or §371 Date</u> | <u>Status or U.S. Patent No.</u> | <u>International Application No.</u> | <u>International Filing Date</u> |
|--|--|--------------------------------------|--|--------------------------------------|
| 08/602,737 | February 21, 1996 | Pending | PCT/EP94/02909 | September 1, 1994 |

I hereby appoint the attorneys and agents associated with Customer No. 001095, respectively and individually, as my attorneys and agents, with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.

Please address all communications to J. Timothy Meigs, Novartis Corporation, Patent and Trademark Dept., P.O. Box 12257, Research Triangle Park, NC 27709-2257.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FIRST JOINT INVENTOR:

Full name : **Hendrik Jan Bosch**

Signature : _____


Date : _____
(MM/DD/YY)

Citizenship : Netherlands

Residence : Oortlaan 20
NL-3572 ZM Utrecht
The Netherlands

SECOND JOINT INVENTOR:

Full name : **Willem Johannes Stiekema**

Signature :  _____

Date : 04/08/98
(MM/DD/YY)

Citizenship : Netherlands

Residence : Leonard Roggeveenstraat 21
NL-6708 SL Wageningen
The Netherlands

IMPORTANT: Before this declaration is signed, the patent application (the specification, the claims and this declaration) must be read and understood by each person signing it, and no changes may be made in the application after this declaration has been signed.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: Bosch, Hendrick J.
Stiekema, Willem J.
- (ii) TITLE OF INVENTION: Hybrid Toxin
- (iii) NUMBER OF SEQUENCES: 15
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: Novartis Corporation
 - (B) STREET: 3054 Cornwallis Road
 - (C) CITY: Research Triangle Park
 - (D) STATE: NC
 - (E) COUNTRY: USA
 - (F) ZIP: 27709
- (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER:
 - (B) FILING DATE:
 - (C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER: US 08/602,737
 - (B) FILING DATE: 21-FEB-1996
- (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: Meigs, J. Timothy
 - (B) REGISTRATION NUMBER: 38,241
 - (C) REFERENCE/DOCKET NUMBER: 130-4080/PCT/CIP
- (ix) TELECOMMUNICATION INFORMATION:
 - (A) TELEPHONE: 919-541-8587
 - (B) TELEFAX: 919-541-8689

(2) INFORMATION FOR SEQ ID NO: 1:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 3567 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Bacillus thuringiensis*

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 1..3567

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

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| Met Glu Glu Asn Asn Gln Asn Gln Cys Ile Pro Tyr Asn Cys Leu Ser | |
| 1 5 10 15 | |
| AAT CCT GAA GAA GTA CTT TTG GAT GGA GAA CGG ATA TCA ACT GGT AAT | 96 |
| Asn Pro Glu Glu Val Leu Leu Asp Gly Glu Arg Ile Ser Thr Gly Asn | |
| 20 25 30 | |
| TCA TCA ATT GAT ATT TCT CTG TCA CTT GTT CAG TTT CTG GTA TCT AAC | 144 |
| Ser Ser Ile Asp Ile Ser Leu Ser Leu Val Gln Phe Leu Val Ser Asn | |
| 35 40 45 | |
| TTT GTA CCA GGG GGA GGA TTT TTA GTT GGA TTA ATA GAT TTT GTA TGG | 192 |
| Phe Val Pro Gly Gly Gly Phe Leu Val Gly Leu Ile Asp Phe Val Trp | |
| 50 55 60 | |
| GGA ATA GTT GGC CCT TCT CAA TGG GAT GCA TTT CTA GTA CAA ATT GAA | 240 |
| Gly Ile Val Gly Pro Ser Gln Trp Asp Ala Phe Leu Val Gln Ile Glu | |
| 65 70 75 80 | |
| CAA TTA ATT AAT GAA AGA ATA GCT GAA TTT GCT AGG AAT GCT GCT ATT | 288 |
| Gln Leu Ile Asn Glu Arg Ile Ala Glu Phe Ala Arg Asn Ala Ala Ile | |
| 85 90 95 | |
| GCT AAT TTA GAA GGA TTA GGA AAC AAT TTC AAT ATA TAT GTG GAA GCA | 336 |
| Ala Asn Leu Glu Gly Leu Gly Asn Asn Phe Asn Ile Tyr Val Glu Ala | |
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| Phe Lys Glu Trp Glu Glu Asp Pro Asn Asn Pro Glu Thr Arg Thr Arg | |
| 115 120 125 | |
| GTA ATT GAT CGC TTT CGT ATA CTT GAT GGG CTA CTT GAA AGG GAC ATT | 432 |
| Val Ile Asp Arg Phe Arg Ile Leu Asp Gly Leu Leu Glu Arg Asp Ile | |
| 130 135 140 | |
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165 170 175

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180 185 190

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Asn Arg Leu Ile Arg His Ile Asp Glu Tyr Ala Asp His Cys Ala Asn
195 200 205

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TGG ATA ACA TAT AAT CGA TTA CGG AGA GAC TTA ACA TTG ACT GTA TTA 720
Trp Ile Thr Tyr Asn Arg Leu Arg Arg Asp Leu Thr Leu Thr Val Leu
225 230 235 240

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Asp Ile Ala Ala Phe Phe Pro Asn Tyr Asp Asn Arg Arg Tyr Pro Ile
245 250 255

CAG CCA GTT GGT CAA CTA ACA AGG GAA GTT TAT ACG GAC CCA TTA ATT 816
Gln Pro Val Gly Gln Leu Thr Arg Glu Val Tyr Thr Asp Pro Leu Ile
260 265 270

AAT TTT AAT CCA CAG TTA CAG TCT GTA GCT CAA TTA CCT ACT TTT AAC 864
Asn Phe Asn Pro Gln Leu Gln Ser Val Ala Gln Leu Pro Thr Phe Asn
275 280 285

GTT ATG GAG AGC AGC GCA ATT AGA AAT CCT CAT TTA TTT GAT ATA TTG 912
Val Met Glu Ser Ser Ala Ile Arg Asn Pro His Leu Phe Asp Ile Leu
290 295 300

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Asn Asn Leu Thr Ile Phe Thr Asp Trp Phe Ser Val Gly Arg Asn Phe
305 310 315 320

TAT TGG GGA GGA CAT CGA GTA ATA TCT AGC CTT ATA GGA GGT GGT AAC 1008
Tyr Trp Gly Gly His Arg Val Ile Ser Ser Leu Ile Gly Gly Gly Asn
325 330 335

ATA ACA TCT CCT ATA TAT GGA AGA GAG GCG AAC CAG GAG CCT CCA AGA 1056
Ile Thr Ser Pro Ile Tyr Gly Arg Glu Ala Asn Gln Glu Pro Pro Arg
340 345 350

TCC TTT ACT TTT AAT GGA CCG GTA TTT AGG ACT TTA TCA AAT CCT ACT 1104
Ser Phe Thr Phe Asn Gly Pro Val Phe Arg Thr Leu Ser Asn Pro Thr

| | | | |
|---|-----|-----|------|
| 355 | 360 | 365 | |
| TTA CGA TTA TTA CAG CAA CCT TGG CCA GCG CCA CCA TTT AAT TTA CGT | | | 1152 |
| Leu Arg Leu Leu Gln Gln Pro Trp Pro Ala Pro Pro Phe Asn Leu Arg | | | |
| 370 | 375 | 380 | |
| GGT GTT GAA GGA GTA GAA TTT TCT ACA CCT ACA AAT AGC TTT ACG TAT | | | 1200 |
| Gly Val Glu Gly Val Glu Phe Ser Thr Pro Thr Asn Ser Phe Thr Tyr | | | |
| 385 | 390 | 395 | 400 |
| CGA GGA AGA GGT ACG GTT GAT TCT TTA ACT GAA TTA CCG CCT GAG GAT | | | 1248 |
| Arg Gly Arg Gly Thr Val Asp Ser Leu Thr Glu Leu Pro Pro Glu Asp | | | |
| 405 | 410 | 415 | |
| AAT AGT GTG CCA CCT CGC GAA GGA TAT AGT CAT CGT TTA TGT CAT GCA | | | 1296 |
| Asn Ser Val Pro Pro Arg Glu Gly Tyr Ser His Arg Leu Cys His Ala | | | |
| 420 | 425 | 430 | |
| ACT TTT GTT CAA AGA TCT GGA ACA CCT TTT TTA ACA ACT GGT GTA GTA | | | 1344 |
| Thr Phe Val Gln Arg Ser Gly Thr Pro Phe Leu Thr Thr Gly Val Val | | | |
| 435 | 440 | 445 | |
| TTT TCT TGG ACG CAT CGT AGT GCA ACT CTT ACA AAT ACA ATT GAT CCA | | | 1392 |
| Phe Ser Trp Thr His Arg Ser Ala Thr Leu Thr Asn Thr Ile Asp Pro | | | |
| 450 | 455 | 460 | |
| GAG AGA ATT AAT CAA ATA CCT TTA GTG AAA GGA TTT AGA GTT TGG GGG | | | 1440 |
| Glu Arg Ile Asn Gln Ile Pro Leu Val Lys Gly Phe Arg Val Trp Gly | | | |
| 465 | 470 | 475 | 480 |
| GGC ACC TCT GTC ATT ACA GGA CCA GGA TTT ACA GGA GGG GAT ATC CTT | | | 1488 |
| Gly Thr Ser Val Ile Thr Gly Pro Gly Phe Thr Gly Gly Asp Ile Leu | | | |
| 485 | 490 | 495 | |
| CGA AGA AAT ACC TTT GGT GAT TTT GTA TCT CTA CAA GTC AAT ATT AAT | | | 1536 |
| Arg Arg Asn Thr Phe Gly Asp Phe Val Ser Leu Gln Val Asn Ile Asn | | | |
| 500 | 505 | 510 | |
| TCA CCA ATT ACC CAA AGA TAC CGT TTA AGA TTT CGT TAC GCT TCC AGT | | | 1584 |
| Ser Pro Ile Thr Gln Arg Tyr Arg Leu Arg Phe Arg Tyr Ala Ser Ser | | | |
| 515 | 520 | 525 | |
| AGG GAT GCA CGA GTT ATA GTA TTA ACA GGA GCG GCA TCC ACA GGA GTG | | | 1632 |
| Arg Asp Ala Arg Val Ile Val Leu Thr Gly Ala Ala Ser Thr Gly Val | | | |
| 530 | 535 | 540 | |
| GGA GGC CAA GTT AGT GTA AAT ATG CCT CTT CAG AAA ACT ATG GAA ATA | | | 1680 |
| Gly Gly Gln Val Ser Val Asn Met Pro Leu Gln Lys Thr Met Glu Ile | | | |
| 545 | 550 | 555 | 560 |
| GGG GAG AAC TTA ACA TCT AGA ACA TTT AGA TAT ACC GAT TTT AGT AAT | | | 1728 |
| Gly Glu Asn Leu Thr Ser Arg Thr Phe Arg Tyr Thr Asp Phe Ser Asn | | | |
| 565 | 570 | 575 | |

CCT TTT TCA TTT AGA GCT AAT CCA GAT ATA ATT GGG ATA AGT GAA CAA 1776
 Pro Phe Ser Phe Arg Ala Asn Pro Asp Ile Ile Gly Ile Ser Glu Gln
 580 585 590

CCT CTA TTT GGT GCA GGT TCT ATT AGT AGC GGT GAA CTT TAT ATA GAT 1824
 Pro Leu Phe Gly Ala Gly Ser Ile Ser Ser Gly Glu Leu Tyr Ile Asp
 595 600 605

AAA ATT GAA ATT ATT CTA GCA GAT GCA ACA TTT GAA GCA GAA TCT GAT 1872
 Lys Ile Glu Ile Ile Leu Ala Asp Ala Thr Phe Glu Ala Glu Ser Asp
 610 615 620

TTA GAA AGA GCA CAA AAG GCG GTG AAT GCC CTG TTT ACT TCT TCC AAT 1920
 Leu Glu Arg Ala Gln Lys Ala Val Asn Ala Leu Phe Thr Ser Ser Asn
 625 630 635 640

CAA ATC GGG TTA AAA ACC GAT GTG ACG GAT TAT CAT ATT GAT CAA GTA 1968
 Gln Ile Gly Leu Lys Thr Asp Val Thr Asp Tyr His Ile Asp Gln Val
 645 650 655

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 Ser Asn Leu Val Asp Cys Leu Ser Asp Glu Phe Cys Leu Asp Glu Lys
 660 665 670

CGA GAA TTG TCC GAG AAA GTC AAA CAT GCG AAG CGA CTC AGT GAT GAG 2064
 Arg Glu Leu Ser Glu Lys Val Lys His Ala Lys Arg Leu Ser Asp Glu
 675 680 685

CGG AAT TTA CTT CAA GAT CCA AAC TTC AGA GGG ATC AAT AGA CAA CCA 2112
 Arg Asn Leu Leu Gln Asp Pro Asn Phe Arg Gly Ile Asn Arg Gln Pro
 690 695 700

GAC CGT GGC TGG AGA GGA AGT ACA GAT ATT ACC ATC CAA GGA GGA GAT 2160
 Asp Arg Gly Trp Arg Gly Ser Thr Asp Ile Thr Ile Gln Gly Gly Asp
 705 710 715 720

GAC GTA TTC AAA GAG AAT TAC GTC ACA CTA CCG GGT ACC GTT GAT GAG 2208
 Asp Val Phe Lys Glu Asn Tyr Val Thr Leu Pro Gly Thr Val Asp Glu
 725 730 735

TGC TAT CCA ACG TAT TTA TAT CAG AAA ATA GAT GAG TCG AAA TTA AAA 2256
 Cys Tyr Pro Thr Tyr Leu Tyr Gln Lys Ile Asp Glu Ser Lys Leu Lys
 740 745 750

GCT TAT ACC CGT TAT GAA TTA AGA GGG TAT ATC GAA GAT AGT CAA GAC 2304
 Ala Tyr Thr Arg Tyr Glu Leu Arg Gly Tyr Ile Glu Asp Ser Gln Asp
 755 760 765

TTA GAA ATC TAT TTG ATC CGT TAC AAT GCA AAA CAC GAA ATA GTA AAT 2352
 Leu Glu Ile Tyr Leu Ile Arg Tyr Asn Ala Lys His Glu Ile Val Asn
 770 775 780

GTG CCA GGC ACG GGT TCC TTA TGG CCG CTT TCA GCC CAA AGT CCA ATC 2400
 Val Pro Gly Thr Gly Ser Leu Trp Pro Leu Ser Ala Gln Ser Pro Ile
 785 790 795 800

GGA AAG TGT GGA GAA CCG AAT CGA TGC GCG CCA CAC CTT GAA TGG AAT 2448
 Gly Lys Cys Gly Glu Pro Asn Arg Cys Ala Pro His Leu Glu Trp Asn
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 Pro Asp Leu Asp Cys Ser Cys Arg Asp Gly Glu Lys Cys Ala His His
 820 825 830

TCC CAT CAT TTC ACC TTG GAT ATT GAT GTT GGA TGT ACA GAC TTA AAT 2544
 Ser His His Phe Thr Leu Asp Ile Asp Val Gly Cys Thr Asp Leu Asn
 835 840 845

GAG GAC TTA GGT GTA TGG GTG ATA TTC AAG ATT AAG ACG CAA GAT GGC 2592
 Glu Asp Leu Gly Val Trp Val Ile Phe Lys Ile Lys Thr Gln Asp Gly
 850 855 860

CAT GCA AGA CTA GGG AAT CTA GAG TTT CTC GAA GAG AAA CCA TTA TTA 2640
 His Ala Arg Leu Gly Asn Leu Glu Phe Leu Glu Glu Lys Pro Leu Leu
 865 870 875 880

GGG GAA GCA CTA GCT CGT GTG AAA AGA GCG GAG AAG AAG TGG AGA GAC 2688
 Gly Glu Ala Leu Ala Arg Val Lys Arg Ala Glu Lys Lys Trp Arg Asp
 885 890 895

AAA CGA GAG AAA CTG CAG TTG GAA ACA AAT ATT GTT TAT AAA GAG GCA 2736
 Lys Arg Glu Lys Leu Gln Leu Glu Thr Asn Ile Val Tyr Lys Glu Ala
 900 905 910

AAA GAA TCT GTA GAT GCT TTA TTT GTA AAC TCT CAA TAT GAT AGA TTA 2784
 Lys Glu Ser Val Asp Ala Leu Phe Val Asn Ser Gln Tyr Asp Arg Leu
 915 920 925

CAA GTG GAT ACG AAC ATC GCG ATG ATT CAT GCG GCA GAT AAA CGC GTT 2832
 Gln Val Asp Thr Asn Ile Ala Met Ile His Ala Ala Asp Lys Arg Val
 930 935 940

CAT AGA ATC CGG GAA GCG TAT CTG CCA GAG TTG TCT GTG ATT CCA GGT 2880
 His Arg Ile Arg Glu Ala Tyr Leu Pro Glu Leu Ser Val Ile Pro Gly
 945 950 955 960

GTC AAT GCG GCC ATT TTC GAA GAA TTA GAG GGA CGT ATT TTT ACA GCG 2928
 Val Asn Ala Ala Ile Phe Glu Glu Leu Glu Gly Arg Ile Phe Thr Ala
 965 970 975

TAT TCC TTA TAT GAT GCG AGA AAT GTC ATT AAA AAT GGC GAT TTC AAT 2976
 Tyr Ser Leu Tyr Asp Ala Arg Asn Val Ile Lys Asn Gly Asp Phe Asn
 980 985 990

AAT GGC TTA TTA TGC TGG AAC GTG AAA GGT CAT GTA GAT GTA GAA GAG 3024

Asn Gly Leu Leu Cys Trp Asn Val Lys Gly His Val Asp Val Glu Glu
995 1000 1005

CAA AAC AAC CAC CGT TCG GTC CTT GTT ATC CCA GAA TGG GAG GCA GAA 3072
Gln Asn Asn His Arg Ser Val Leu Val Ile Pro Glu Trp Glu Ala Glu
1010 1015 1020

GTG TCA CAA GAG GTT CGT GTC TGT CCA GGT CGT GGC TAT ATC CTT CGT 3120
Val Ser Gln Glu Val Arg Val Cys Pro Gly Arg Gly Tyr Ile Leu Arg
1025 1030 1035 1040

GTC ACA GCA TAT AAA GAG GGA TAT GGA GAG GGC TGC GTA ACG ATC CAT 3168
Val Thr Ala Tyr Lys Glu Gly Tyr Gly Glu Gly Cys Val Thr Ile His
1045 1050 1055

GAG ATC GAA GAC AAT ACA GAC GAA CTG AAA TTC AGC AAC TGT GTA GAA 3216
Glu Ile Glu Asp Asn Thr Asp Glu Leu Lys Phe Ser Asn Cys Val Glu
1060 1065 1070

GAG GAA GTA TAT CCA AAC AAC ACA GTA ACG TGT AAT AAT TAT ACT GGG 3264
Glu Glu Val Tyr Pro Asn Asn Thr Val Thr Cys Asn Asn Tyr Thr Gly
1075 1080 1085

ACT CAA GAA GAA TAT GAG GGT ACG TAC ACT TCT CGT AAT CAA GGA TAT 3312
Thr Gln Glu Glu Tyr Glu Gly Thr Tyr Thr Ser Arg Asn Gln Gly Tyr
1090 1095 1100

GAC GAA GCC TAT GGT AAT AAC CCT TCC GTA CCA GCT GAT TAC GCT TCA 3360
Asp Glu Ala Tyr Gly Asn Asn Pro Ser Val Pro Ala Asp Tyr Ala Ser
1105 1110 1115 1120

GTC TAT GAA GAA AAA TCG TAT ACA GAT GGA CGA AGA GAG AAT CCT TGT 3408
Val Tyr Glu Glu Lys Ser Tyr Thr Asp Gly Arg Arg Glu Asn Pro Cys
1125 1130 1135

GAA TCT AAC AGA GGC TAT GGG GAT TAC ACA CCA CTA CCG GCT GGT TAT 3456
Glu Ser Asn Arg Gly Tyr Gly Asp Tyr Thr Pro Leu Pro Ala Gly Tyr
1140 1145 1150

GTA ACA AAG GAT TTA GAG TAC TTC CCA GAG ACC GAT AAG GTA TGG ATT 3504
Val Thr Lys Asp Leu Glu Tyr Phe Pro Glu Thr Asp Lys Val Trp Ile
1155 1160 1165

GAG ATC GGA GAA ACA GAA GGA ACA TTC ATC GTG GAT AGC GTG GAA TTA 3552
Glu Ile Gly Glu Thr Glu Gly Thr Phe Ile Val Asp Ser Val Glu Leu
1170 1175 1180

CTC CTT ATG GAG GAA 3567
Leu Leu Met Glu Glu
1185

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1189 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

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Met Glu Glu Asn Asn Gln Asn Gln Cys Ile Pro Tyr Asn Cys Leu Ser
 1             5             10             15

Asn Pro Glu Glu Val Leu Leu Asp Gly Glu Arg Ile Ser Thr Gly Asn
      20             25             30

Ser Ser Ile Asp Ile Ser Leu Ser Leu Val Gln Phe Leu Val Ser Asn
      35             40             45

Phe Val Pro Gly Gly Gly Phe Leu Val Gly Leu Ile Asp Phe Val Trp
      50             55             60

Gly Ile Val Gly Pro Ser Gln Trp Asp Ala Phe Leu Val Gln Ile Glu
      65             70             75             80

Gln Leu Ile Asn Glu Arg Ile Ala Glu Phe Ala Arg Asn Ala Ala Ile
      85             90             95

Ala Asn Leu Glu Gly Leu Gly Asn Asn Phe Asn Ile Tyr Val Glu Ala
      100            105            110

Phe Lys Glu Trp Glu Glu Asp Pro Asn Asn Pro Glu Thr Arg Thr Arg
      115            120            125

Val Ile Asp Arg Phe Arg Ile Leu Asp Gly Leu Leu Glu Arg Asp Ile
      130            135            140

Pro Ser Phe Arg Ile Ser Gly Phe Glu Val Pro Leu Leu Ser Val Tyr
      145            150            155            160

Ala Gln Ala Ala Asn Leu His Leu Ala Ile Leu Arg Asp Ser Val Ile
      165            170            175

Phe Gly Glu Arg Trp Gly Leu Thr Thr Ile Asn Val Asn Glu Asn Tyr
      180            185            190

Asn Arg Leu Ile Arg His Ile Asp Glu Tyr Ala Asp His Cys Ala Asn
      195            200            205

Thr Tyr Asn Arg Gly Leu Asn Asn Leu Pro Lys Ser Thr Tyr Gln Asp
      210            215            220

Trp Ile Thr Tyr Asn Arg Leu Arg Arg Asp Leu Thr Leu Thr Val Leu

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| | | | |
|---|-----|-----|-----|
| 225 | 230 | 235 | 240 |
| Asp Ile Ala Ala Phe Phe Pro Asn Tyr Asp Asn Arg Arg Tyr Pro Ile | 245 | 250 | 255 |
| Gln Pro Val Gly Gln Leu Thr Arg Glu Val Tyr Thr Asp Pro Leu Ile | 260 | 265 | 270 |
| Asn Phe Asn Pro Gln Leu Gln Ser Val Ala Gln Leu Pro Thr Phe Asn | 275 | 280 | 285 |
| Val Met Glu Ser Ser Ala Ile Arg Asn Pro His Leu Phe Asp Ile Leu | 290 | 295 | 300 |
| Asn Asn Leu Thr Ile Phe Thr Asp Trp Phe Ser Val Gly Arg Asn Phe | 305 | 310 | 315 |
| Tyr Trp Gly Gly His Arg Val Ile Ser Ser Leu Ile Gly Gly Gly Asn | 325 | 330 | 335 |
| Ile Thr Ser Pro Ile Tyr Gly Arg Glu Ala Asn Gln Glu Pro Pro Arg | 340 | 345 | 350 |
| Ser Phe Thr Phe Asn Gly Pro Val Phe Arg Thr Leu Ser Asn Pro Thr | 355 | 360 | 365 |
| Leu Arg Leu Leu Gln Gln Pro Trp Pro Ala Pro Pro Phe Asn Leu Arg | 370 | 375 | 380 |
| Gly Val Glu Gly Val Glu Phe Ser Thr Pro Thr Asn Ser Phe Thr Tyr | 385 | 390 | 395 |
| Arg Gly Arg Gly Thr Val Asp Ser Leu Thr Glu Leu Pro Pro Glu Asp | 405 | 410 | 415 |
| Asn Ser Val Pro Pro Arg Glu Gly Tyr Ser His Arg Leu Cys His Ala | 420 | 425 | 430 |
| Thr Phe Val Gln Arg Ser Gly Thr Pro Phe Leu Thr Thr Gly Val Val | 435 | 440 | 445 |
| Phe Ser Trp Thr His Arg Ser Ala Thr Leu Thr Asn Thr Ile Asp Pro | 450 | 455 | 460 |
| Glu Arg Ile Asn Gln Ile Pro Leu Val Lys Gly Phe Arg Val Trp Gly | 465 | 470 | 475 |
| Gly Thr Ser Val Ile Thr Gly Pro Gly Phe Thr Gly Gly Asp Ile Leu | 485 | 490 | 495 |
| Arg Arg Asn Thr Phe Gly Asp Phe Val Ser Leu Gln Val Asn Ile Asn | 500 | 505 | 510 |

Ser Pro Ile Thr Gln Arg Tyr Arg Leu Arg Phe Arg Tyr Ala Ser Ser
 515 520 525
 Arg Asp Ala Arg Val Ile Val Leu Thr Gly Ala Ala Ser Thr Gly Val
 530 535 540
 Gly Gly Gln Val Ser Val Asn Met Pro Leu Gln Lys Thr Met Glu Ile
 545 550 555 560
 Gly Glu Asn Leu Thr Ser Arg Thr Phe Arg Tyr Thr Asp Phe Ser Asn
 565 570 575
 Pro Phe Ser Phe Arg Ala Asn Pro Asp Ile Ile Gly Ile Ser Glu Gln
 580 585 590
 Pro Leu Phe Gly Ala Gly Ser Ile Ser Ser Gly Glu Leu Tyr Ile Asp
 595 600 605
 Lys Ile Glu Ile Ile Leu Ala Asp Ala Thr Phe Glu Ala Glu Ser Asp
 610 615 620
 Leu Glu Arg Ala Gln Lys Ala Val Asn Ala Leu Phe Thr Ser Ser Asn
 625 630 635 640
 Gln Ile Gly Leu Lys Thr Asp Val Thr Asp Tyr His Ile Asp Gln Val
 645 650 655
 Ser Asn Leu Val Asp Cys Leu Ser Asp Glu Phe Cys Leu Asp Glu Lys
 660 665 670
 Arg Glu Leu Ser Glu Lys Val Lys His Ala Lys Arg Leu Ser Asp Glu
 675 680 685
 Arg Asn Leu Leu Gln Asp Pro Asn Phe Arg Gly Ile Asn Arg Gln Pro
 690 695 700
 Asp Arg Gly Trp Arg Gly Ser Thr Asp Ile Thr Ile Gln Gly Gly Asp
 705 710 715 720
 Asp Val Phe Lys Glu Asn Tyr Val Thr Leu Pro Gly Thr Val Asp Glu
 725 730 735
 Cys Tyr Pro Thr Tyr Leu Tyr Gln Lys Ile Asp Glu Ser Lys Leu Lys
 740 745 750
 Ala Tyr Thr Arg Tyr Glu Leu Arg Gly Tyr Ile Glu Asp Ser Gln Asp
 755 760 765
 Leu Glu Ile Tyr Leu Ile Arg Tyr Asn Ala Lys His Glu Ile Val Asn
 770 775 780
 Val Pro Gly Thr Gly Ser Leu Trp Pro Leu Ser Ala Gln Ser Pro Ile
 785 790 795 800

Gly Lys Cys Gly Glu Pro Asn Arg Cys Ala Pro His Leu Glu Trp Asn
805 810 815

Pro Asp Leu Asp Cys Ser Cys Arg Asp Gly Glu Lys Cys Ala His His
820 825 830

Ser His His Phe Thr Leu Asp Ile Asp Val Gly Cys Thr Asp Leu Asn
835 840 845

Glu Asp Leu Gly Val Trp Val Ile Phe Lys Ile Lys Thr Gln Asp Gly
850 855 860

His Ala Arg Leu Gly Asn Leu Glu Phe Leu Glu Glu Lys Pro Leu Leu
865 870 875 880

Gly Glu Ala Leu Ala Arg Val Lys Arg Ala Glu Lys Lys Trp Arg Asp
885 890 895

Lys Arg Glu Lys Leu Gln Leu Glu Thr Asn Ile Val Tyr Lys Glu Ala
900 905 910

Lys Glu Ser Val Asp Ala Leu Phe Val Asn Ser Gln Tyr Asp Arg Leu
915 920 925

Gln Val Asp Thr Asn Ile Ala Met Ile His Ala Ala Asp Lys Arg Val
930 935 940

His Arg Ile Arg Glu Ala Tyr Leu Pro Glu Leu Ser Val Ile Pro Gly
945 950 955 960

Val Asn Ala Ala Ile Phe Glu Glu Leu Glu Gly Arg Ile Phe Thr Ala
965 970 975

Tyr Ser Leu Tyr Asp Ala Arg Asn Val Ile Lys Asn Gly Asp Phe Asn
980 985 990

Asn Gly Leu Leu Cys Trp Asn Val Lys Gly His Val Asp Val Glu Glu
995 1000 1005

Gln Asn Asn His Arg Ser Val Leu Val Ile Pro Glu Trp Glu Ala Glu
1010 1015 1020

Val Ser Gln Glu Val Arg Val Cys Pro Gly Arg Gly Tyr Ile Leu Arg
1025 1030 1035 1040

Val Thr Ala Tyr Lys Glu Gly Tyr Gly Glu Gly Cys Val Thr Ile His
1045 1050 1055

Glu Ile Glu Asp Asn Thr Asp Glu Leu Lys Phe Ser Asn Cys Val Glu
1060 1065 1070

Glu Glu Val Tyr Pro Asn Asn Thr Val Thr Cys Asn Asn Tyr Thr Gly

1075 1080 1085

Thr Gln Glu Glu Tyr Glu Gly Thr Tyr Thr Ser Arg Asn Gln Gly Tyr
1090 1095 1100

Asp Glu Ala Tyr Gly Asn Asn Pro Ser Val Pro Ala Asp Tyr Ala Ser
1105 1110 1115 1120

Val Tyr Glu Glu Lys Ser Tyr Thr Asp Gly Arg Arg Glu Asn Pro Cys
1125 1130 1135

Glu Ser Asn Arg Gly Tyr Gly Asp Tyr Thr Pro Leu Pro Ala Gly Tyr
1140 1145 1150

Val Thr Lys Asp Leu Glu Tyr Phe Pro Glu Thr Asp Lys Val Trp Ile
1155 1160 1165

Glu Ile Gly Glu Thr Glu Gly Thr Phe Ile Val Asp Ser Val Glu Leu
1170 1175 1180

Leu Leu Met Glu Glu
1185

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3513 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Bacillus thuringiensis*

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..3513

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

| | |
|--|----|
| ATG GAG ATA GTG AAT AAT CAG AAT CAA TGC GTG CCT TAT AAT TGT TTA | 48 |
| Met Glu Ile Val Asn Asn Gln Asn Gln Cys Val Pro Tyr Asn Cys Leu | |
| 1 5 10 15 | |
| AAT AAT CCT GAA AAT GAG ATA TTA GAT ATT GAA AGG TCA AAT AGT ACT | 96 |
| Asn Asn Pro Glu Asn Glu Ile Leu Asp Ile Glu Arg Ser Asn Ser Thr | |

| 20 | 25 | 30 | |
|---|----|----|-----|
| GTA GCA ACA AAC ATC GCC TTG GAG ATT AGT CGT CTG CTC GCT TCC GCA Val Ala Thr Asn Ile Ala Leu Glu Ile Ser Arg Leu Leu Ala Ser Ala 35 40 45 | | | 144 |
| ACT CCA ATA GGG GGG ATT TTA TTA GGA TTG TTT GAT GCA ATA TGG GGG Thr Pro Ile Gly Gly Ile Leu Leu Gly Leu Phe Asp Ala Ile Trp Gly 50 55 60 | | | 192 |
| TCT ATA GGC CCT TCA CAA TGG GAT TTA TTT TTA GAG CAA ATT GAG CTA Ser Ile Gly Pro Ser Gln Trp Asp Leu Phe Leu Glu Gln Ile Glu Leu 65 70 75 80 | | | 240 |
| TTG ATT GAC CAA AAA ATA GAG GAA TTC GCT AGA AAC CAG GCA ATT TCT Leu Ile Asp Gln Lys Ile Glu Glu Phe Ala Arg Asn Gln Ala Ile Ser 85 90 95 | | | 288 |
| AGA TTG GAA GGG ATA AGC AGT CTG TAC GGA ATT TAT ACA GAA GCT TTT Arg Leu Glu Gly Ile Ser Ser Leu Tyr Gly Ile Tyr Thr Glu Ala Phe 100 105 110 | | | 336 |
| AGA GAG TGG GAA GCA GAT CCT ACT AAT CCA GCA TTA AAA GAA GAG ATG Arg Glu Trp Glu Ala Asp Pro Thr Asn Pro Ala Leu Lys Glu Glu Met 115 120 125 | | | 384 |
| CGT ACT CAA TTT AAT GAC ATG AAC AGT ATT CTT GTA ACA GCT ATT CCT Arg Thr Gln Phe Asn Asp Met Asn Ser Ile Leu Val Thr Ala Ile Pro 130 135 140 | | | 432 |
| CTT TTT TCA GTT CAA AAT TAT CAA GTC CCA TTT TTA TCA GTA TAT GTT Leu Phe Ser Val Gln Asn Tyr Gln Val Pro Phe Leu Ser Val Tyr Val 145 150 155 160 | | | 480 |
| CAA GCT GCA AAT TTA CAT TTA TCG GTT TTG AGA GAT GTT TCA GTG TTT Gln Ala Ala Asn Leu His Leu Ser Val Leu Arg Asp Val Ser Val Phe 165 170 175 | | | 528 |
| GGG CAG GCT TGG GGA TTT GAT ATA GCA ACA ATA AAT AGT CGT TAT AAT Gly Gln Ala Trp Gly Phe Asp Ile Ala Thr Ile Asn Ser Arg Tyr Asn 180 185 190 | | | 576 |
| GAT CTG ACT AGA CTT ATT CCT ATA TAT ACA GAT TAT GCT GTA CGC TGG Asp Leu Thr Arg Leu Ile Pro Ile Tyr Thr Asp Tyr Ala Val Arg Trp 195 200 205 | | | 624 |
| TAC AAT ACG GGA TTA GAT CGC TTA CCA CGA ACT GGT GGG CTG CGA AAC Tyr Asn Thr Gly Leu Asp Arg Leu Pro Arg Thr Gly Gly Leu Arg Asn 210 215 220 | | | 672 |
| TGG GCA AGA TTT AAT CAG TTT AGA AGA GAG TTA ACA ATA TCA GTA TTA Trp Ala Arg Phe Asn Gln Phe Arg Arg Glu Leu Thr Ile Ser Val Leu 225 230 235 240 | | | 720 |

| | |
|---|------|
| GAT ATT ATT TCT TTT TTC AGA AAT TAC GAT TCT AGA TTA TAT CCA ATT | 768 |
| Asp Ile Ile Ser Phe Phe Arg Asn Tyr Asp Ser Arg Leu Tyr Pro Ile | |
| 245 250 255 | |
| CCA ACA AGC TCC CAA TTA ACG CGG GAA GTA TAT ACA GAT CCG GTA ATT | 816 |
| Pro Thr Ser Ser Gln Leu Thr Arg Glu Val Tyr Thr Asp Pro Val Ile | |
| 260 265 270 | |
| AAT ATA ACT GAC TAT AGA GTT GGC CCC AGC TTC GAG AAT ATT GAG AAC | 864 |
| Asn Ile Thr Asp Tyr Arg Val Gly Pro Ser Phe Glu Asn Ile Glu Asn | |
| 275 280 285 | |
| TCA GCC ATT AGA AGC CCC CAC CTT ATG GAC TTC TTA AAT AAT TTG ACC | 912 |
| Ser Ala Ile Arg Ser Pro His Leu Met Asp Phe Leu Asn Asn Leu Thr | |
| 290 295 300 | |
| ATT GAT ACG GAT TTG ATT AGA GGT GTT CAC TAT TGG GCA GGG CAT CGT | 960 |
| Ile Asp Thr Asp Leu Ile Arg Gly Val His Tyr Trp Ala Gly His Arg | |
| 305 310 315 320 | |
| GTA ACT TCT CAT TTT ACA GGT AGT TCT CAA GTG ATA ACA ACC CCT CAA | 1008 |
| Val Thr Ser His Phe Thr Gly Ser Ser Gln Val Ile Thr Thr Pro Gln | |
| 325 330 335 | |
| TAT GGG ATA ACC GCA AAT GCG GAA CCA AGA CGA ACT ATT GCT CCT AGT | 1056 |
| Tyr Gly Ile Thr Ala Asn Ala Glu Pro Arg Arg Thr Ile Ala Pro Ser | |
| 340 345 350 | |
| ACT TTT CCA GGT CTT AAC CTA TTT TAT AGA ACA TTA TCA AAT CCT TTC | 1104 |
| Thr Phe Pro Gly Leu Asn Leu Phe Tyr Arg Thr Leu Ser Asn Pro Phe | |
| 355 360 365 | |
| TTC CGA AGA TCA GAA AAT ATT ACT CCT ACC TTA GGG ATA AAT GTA GTA | 1152 |
| Phe Arg Arg Ser Glu Asn Ile Thr Pro Thr Leu Gly Ile Asn Val Val | |
| 370 375 380 | |
| CAG GGA GTA GGG TTC ATT CAA CCA AAT AAT GCT GAA GTT CTA TAT AGA | 1200 |
| Gln Gly Val Gly Phe Ile Gln Pro Asn Asn Ala Glu Val Leu Tyr Arg | |
| 385 390 395 400 | |
| AGT AGG GGG ACA GTA GAT TCT CTT AAT GAG TTA CCA ATT GAT GGT GAG | 1248 |
| Ser Arg Gly Thr Val Asp Ser Leu Asn Glu Leu Pro Ile Asp Gly Glu | |
| 405 410 415 | |
| AAT TCA TTA GTT GGA TAT AGT CAT CGA TTA AGT CAT GTT ACA CTA ACC | 1296 |
| Asn Ser Leu Val Gly Tyr Ser His Arg Leu Ser His Val Thr Leu Thr | |
| 420 425 430 | |
| AGG TCG TTA TAT AAT ACT AAT ATA ACT AGC CTG CCA ACA TTT GTT TGG | 1344 |
| Arg Ser Leu Tyr Asn Thr Asn Ile Thr Ser Leu Pro Thr Phe Val Trp | |
| 435 440 445 | |

ACA CAT CAC AGT GCT ACT AAT ACA AAT ACA ATT AAT CCA GAT ATT ATT 1392
 Thr His His Ser Ala Thr Asn Thr Asn Thr Ile Asn Pro Asp Ile Ile
 450 455 460

ACA CAA ATA CCT TTA GTG AAA GGA TTT AGA CTT GGT GGT GGC ACC TCT 1440
 Thr Gln Ile Pro Leu Val Lys Gly Phe Arg Leu Gly Gly Gly Thr Ser
 465 470 475 480

GTC ATT AAA GGA CCA GGA TTT ACA GGA GGG GAT ATC CTT CGA AGA AAT 1488
 Val Ile Lys Gly Pro Gly Phe Thr Gly Gly Asp Ile Leu Arg Arg Asn
 485 490 495

ACC ATT GGT GAG TTT GTG TCT TTA CAA GTC AAT ATT AAC TCA CCA ATT 1536
 Thr Ile Gly Glu Phe Val Ser Leu Gln Val Asn Ile Asn Ser Pro Ile
 500 505 510

ACC CAA AGA TAC CGT TTA AGA TTT CGT TAT GCT TCC AGT AGG GAT GCA 1584
 Thr Gln Arg Tyr Arg Leu Arg Phe Arg Tyr Ala Ser Ser Arg Asp Ala
 515 520 525

CGA ATT ACT GTA GCG ATA GGA GGA CAA ATT AGA GTA GAT ATG ACC CTT 1632
 Arg Ile Thr Val Ala Ile Gly Gly Gln Ile Arg Val Asp Met Thr Leu
 530 535 540

GAA AAA ACC ATG GAA ATT GGG GAG AGC TTA ACA TCT AGA ACA TTT AGC 1680
 Glu Lys Thr Met Glu Ile Gly Glu Ser Leu Thr Ser Arg Thr Phe Ser
 545 550 555 560

TAT ACC AAT TTT AGT AAT CCT TTT TCA TTT AGG GCT AAT CCA GAT ATA 1728
 Tyr Thr Asn Phe Ser Asn Pro Phe Ser Phe Arg Ala Asn Pro Asp Ile
 565 570 575

ATT AGA ATA GCT GAA GAA CTT CCT ATT CGT GGT GGT GAG CTT TAT ATA 1776
 Ile Arg Ile Ala Glu Glu Leu Pro Ile Arg Gly Gly Glu Leu Tyr Ile
 580 585 590

GAT AAA ATT GAA CTT ATT CTA GCA GAT GCA ACA TTT GAA GAA GAA TAT 1824
 Asp Lys Ile Glu Leu Ile Leu Ala Asp Ala Thr Phe Glu Glu Glu Tyr
 595 600 605

GAT TTG GAA AGA GCA CAG AAG GCG GTG AAT GCC CTG TTT ACT TCT ACA 1872
 Asp Leu Glu Arg Ala Gln Lys Ala Val Asn Ala Leu Phe Thr Ser Thr
 610 615 620

AAT CAA CTA GGG CTA AAA ACA GAT GTG ACG GAT TAT CAT ATT GAT CAA 1920
 Asn Gln Leu Gly Leu Lys Thr Asp Val Thr Asp Tyr His Ile Asp Gln
 625 630 635 640

GTT TCC AAT TTA GTT GAG TGT TTA TCG GAT GAA TTT TGT CTG GAT GAA 1968
 Val Ser Asn Leu Val Glu Cys Leu Ser Asp Glu Phe Cys Leu Asp Glu
 645 650 655

AAG AGA GAA TTA TCC GAG AAA GTC AAA CAT GCG AAG CGA CTC AGT GAT 2016

| | |
|---|------|
| Lys Arg Glu Leu Ser Glu Lys Val Lys His Ala Lys Arg Leu Ser Asp | |
| 660 665 670 | |
| GAA CGG AAT TTA CTT CAA GAT CCA AAC TTC AGA GGG ATC AAT AGG CAA | 2064 |
| Glu Arg Asn Leu Leu Gln Asp Pro Asn Phe Arg Gly Ile Asn Arg Gln | |
| 675 680 685 | |
| CCA GAC CGT GGC TGG AGA GGA AGC ACG GAT ATT ACT ATC CAA GGT GGA | 2112 |
| Pro Asp Arg Gly Trp Arg Gly Ser Thr Asp Ile Thr Ile Gln Gly Gly | |
| 690 695 700 | |
| GAT GAC GTA TTC AAA GAG AAT TAC GTC ACA TTA CCG GGT ACC TTT GAT | 2160 |
| Asp Asp Val Phe Lys Glu Asn Tyr Val Thr Leu Pro Gly Thr Phe Asp | |
| 705 710 715 720 | |
| GAG TGC TAT CCA ACG TAT TTA TAT CAA AAA ATA GAT GAG TCG AAG TTA | 2208 |
| Glu Cys Tyr Pro Thr Tyr Leu Tyr Gln Lys Ile Asp Glu Ser Lys Leu | |
| 725 730 735 | |
| AAA GCT TAT ACC CGC TAT GAA TTA AGA GGG TAT ATC GAG GAT AGT CAA | 2256 |
| Lys Ala Tyr Thr Arg Tyr Glu Leu Arg Gly Tyr Ile Glu Asp Ser Gln | |
| 740 745 750 | |
| GAC TTA GAA ATC TAT TTA ATT CGC TAC AAT GCA AAA CAC GAG ACA GTA | 2304 |
| Asp Leu Glu Ile Tyr Leu Ile Arg Tyr Asn Ala Lys His Glu Thr Val | |
| 755 760 765 | |
| AAC GTG CCA GGT ACG GGT TCC TTA TGG CCG CTT TCA GCC CAA AGT CCA | 2352 |
| Asn Val Pro Gly Thr Gly Ser Leu Trp Pro Leu Ser Ala Gln Ser Pro | |
| 770 775 780 | |
| ATC GGA AAG TGT GGA GAA CCG AAT CGA TGC GCG CCA CAC CTT GAA TGG | 2400 |
| Ile Gly Lys Cys Gly Glu Pro Asn Arg Cys Ala Pro His Leu Glu Trp | |
| 785 790 795 800 | |
| AAT CCT AAT CTA GAT TGC TCC TGC AGA GAC GGG GAA AAA TGT GCC CAT | 2448 |
| Asn Pro Asn Leu Asp Cys Ser Cys Arg Asp Gly Glu Lys Cys Ala His | |
| 805 810 815 | |
| CAT TCC CAT CAT TTC TCC TTG GAC ATT GAT GTT GGA TGT ACA GAC TTA | 2496 |
| His Ser His His Phe Ser Leu Asp Ile Asp Val Gly Cys Thr Asp Leu | |
| 820 825 830 | |
| AAT GAG GAC TTA GGT GTA TGG GTG ATA TTC AAG ATT AAG ACA CAA GAT | 2544 |
| Asn Glu Asp Leu Gly Val Trp Val Ile Phe Lys Ile Lys Thr Gln Asp | |
| 835 840 845 | |
| GGC TAT GCA AGA CTA GGA AAT CTA GAG TTT CTC GAA GAG AAC CCA CTA | 2592 |
| Gly Tyr Ala Arg Leu Gly Asn Leu Glu Phe Leu Glu Glu Asn Pro Leu | |
| 850 855 860 | |
| TTA GGG GAA GCA CTA GCT CGT GTG AAA AGA GCG GAG AAA AAA TGG AGA | 2640 |
| Leu Gly Glu Ala Leu Ala Arg Val Lys Arg Ala Glu Lys Lys Trp Arg | |

37

TAT GAC GAA GCC TAT GAA AGC AAT TCT TCT GTA CAT GCG TCA GTC TAT 3312
 Tyr Asp Glu Ala Tyr Glu Ser Asn Ser Ser Val His Ala Ser Val Tyr
 1090 1095 1100

 GAA GAA AAA TCG TAT ACA GAT AGA CGA AGA GAG AAT CCT TGT GAA TCT 3360
 Glu Glu Lys Ser Tyr Thr Asp Arg Arg Arg Glu Asn Pro Cys Glu Ser
 1105 1110 1115 1120

 AAC AGA GGA TAT GGG GAT TAC ACA CCA CTA CCA GCT GGC TAT GTG ACA 3408
 Asn Arg Gly Tyr Gly Asp Tyr Thr Pro Leu Pro Ala Gly Tyr Val Thr
 1125 1130 1135

 AAA GAA TTA GAG TAC TTC CCA GAA ACC GAT AAG GTA TGG ATT GAG ATC 3456
 Lys Glu Leu Glu Tyr Phe Pro Glu Thr Asp Lys Val Trp Ile Glu Ile
 1140 1145 1150

 GGA GAA ACG GAA GGA ACA TTC ATC GTG GAC AGC GTG GAA TTA CTT CTT 3504
 Gly Glu Thr Glu Gly Thr Phe Ile Val Asp Ser Val Glu Leu Leu Leu
 1155 1160 1165

 ATG GAG GAA 3513
 Met Glu Glu
 1170

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1171 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Met Glu Ile Val Asn Asn Gln Asn Gln Cys Val Pro Tyr Asn Cys Leu
 1 5 10 15

 Asn Asn Pro Glu Asn Glu Ile Leu Asp Ile Glu Arg Ser Asn Ser Thr
 20 25 30

 Val Ala Thr Asn Ile Ala Leu Glu Ile Ser Arg Leu Leu Ala Ser Ala
 35 40 45

 Thr Pro Ile Gly Gly Ile Leu Leu Gly Leu Phe Asp Ala Ile Trp Gly
 50 55 60

 Ser Ile Gly Pro Ser Gln Trp Asp Leu Phe Leu Glu Gln Ile Glu Leu
 65 70 75 80

 Leu Ile Asp Gln Lys Ile Glu Glu Phe Ala Arg Asn Gln Ala Ile Ser

39

Phe Arg Arg Ser Glu Asn Ile Thr Pro Thr Leu Gly Ile Asn Val Val
 370 375 380
 Gln Gly Val Gly Phe Ile Gln Pro Asn Asn Ala Glu Val Leu Tyr Arg
 385 390 395 400
 Ser Arg Gly Thr Val Asp Ser Leu Asn Glu Leu Pro Ile Asp Gly Glu
 405 410 415
 Asn Ser Leu Val Gly Tyr Ser His Arg Leu Ser His Val Thr Leu Thr
 420 425 430
 Arg Ser Leu Tyr Asn Thr Asn Ile Thr Ser Leu Pro Thr Phe Val Trp
 435 440 445
 Thr His His Ser Ala Thr Asn Thr Asn Thr Ile Asn Pro Asp Ile Ile
 450 455 460
 Thr Gln Ile Pro Leu Val Lys Gly Phe Arg Leu Gly Gly Gly Thr Ser
 465 470 475 480
 Val Ile Lys Gly Pro Gly Phe Thr Gly Gly Asp Ile Leu Arg Arg Asn
 485 490 495
 Thr Ile Gly Glu Phe Val Ser Leu Gln Val Asn Ile Asn Ser Pro Ile
 500 505 510
 Thr Gln Arg Tyr Arg Leu Arg Phe Arg Tyr Ala Ser Ser Arg Asp Ala
 515 520 525
 Arg Ile Thr Val Ala Ile Gly Gly Gln Ile Arg Val Asp Met Thr Leu
 530 535 540
 Glu Lys Thr Met Glu Ile Gly Glu Ser Leu Thr Ser Arg Thr Phe Ser
 545 550 555 560
 Tyr Thr Asn Phe Ser Asn Pro Phe Ser Phe Arg Ala Asn Pro Asp Ile
 565 570 575
 Ile Arg Ile Ala Glu Glu Leu Pro Ile Arg Gly Gly Glu Leu Tyr Ile
 580 585 590
 Asp Lys Ile Glu Leu Ile Leu Ala Asp Ala Thr Phe Glu Glu Glu Tyr
 595 600 605
 Asp Leu Glu Arg Ala Gln Lys Ala Val Asn Ala Leu Phe Thr Ser Thr
 610 615 620
 Asn Gln Leu Gly Leu Lys Thr Asp Val Thr Asp Tyr His Ile Asp Gln
 625 630 635 640
 Val Ser Asn Leu Val Glu Cys Leu Ser Asp Glu Phe Cys Leu Asp Glu
 645 650 655

Lys Arg Glu Leu Ser Glu Lys Val Lys His Ala Lys Arg Leu Ser Asp
 660 665 670
 Glu Arg Asn Leu Leu Gln Asp Pro Asn Phe Arg Gly Ile Asn Arg Gln
 675 680 685
 Pro Asp Arg Gly Trp Arg Gly Ser Thr Asp Ile Thr Ile Gln Gly Gly
 690 695 700
 Asp Asp Val Phe Lys Glu Asn Tyr Val Thr Leu Pro Gly Thr Phe Asp
 705 710 715 720
 Glu Cys Tyr Pro Thr Tyr Leu Tyr Gln Lys Ile Asp Glu Ser Lys Leu
 725 730 735
 Lys Ala Tyr Thr Arg Tyr Glu Leu Arg Gly Tyr Ile Glu Asp Ser Gln
 740 745 750
 Asp Leu Glu Ile Tyr Leu Ile Arg Tyr Asn Ala Lys His Glu Thr Val
 755 760 765
 Asn Val Pro Gly Thr Gly Ser Leu Trp Pro Leu Ser Ala Gln Ser Pro
 770 775 780
 Ile Gly Lys Cys Gly Glu Pro Asn Arg Cys Ala Pro His Leu Glu Trp
 785 790 795 800
 Asn Pro Asn Leu Asp Cys Ser Cys Arg Asp Gly Glu Lys Cys Ala His
 805 810 815
 His Ser His His Phe Ser Leu Asp Ile Asp Val Gly Cys Thr Asp Leu
 820 825 830
 Asn Glu Asp Leu Gly Val Trp Val Ile Phe Lys Ile Lys Thr Gln Asp
 835 840 845
 Gly Tyr Ala Arg Leu Gly Asn Leu Glu Phe Leu Glu Glu Asn Pro Leu
 850 855 860
 Leu Gly Glu Ala Leu Ala Arg Val Lys Arg Ala Glu Lys Lys Trp Arg
 865 870 875 880
 Asp Lys Cys Glu Lys Leu Glu Trp Glu Thr Asn Ile Val Tyr Lys Glu
 885 890 895
 Ala Lys Glu Ser Val Asp Ala Leu Phe Val Asn Ser Gln Tyr Asp Arg
 900 905 910
 Leu Gln Ala Asp Thr Asn Ile Ala Met Ile His Ala Ala Asp Lys Arg
 915 920 925
 Val His Ser Ile Arg Glu Ala Tyr Leu Pro Glu Leu Ser Val Ile Pro

930 935 940
 Gly Val Asn Ala Ala Ile Phe Glu Glu Leu Glu Gly Arg Ile Phe Thr
 945 950 955 960
 Ala Phe Ser Leu Tyr Asp Ala Arg Asn Val Ile Lys Asn Gly Asp Phe
 965 970 975
 Asn Asn Gly Leu Ser Cys Trp Asn Val Lys Gly His Val Asp Val Glu
 980 985 990
 Glu Gln Asn Asn His Arg Ser Val Leu Val Val Pro Glu Trp Glu Ala
 995 1000 1005
 Glu Val Ser Gln Glu Val Arg Val Cys Pro Gly Arg Gly Tyr Ile Leu
 1010 1015 1020
 Arg Val Thr Ala Tyr Lys Glu Gly Tyr Gly Glu Gly Cys Val Thr Ile
 1025 1030 1035 1040
 His Glu Ile Glu Asp Asn Thr Asp Glu Leu Lys Phe Ser Asn Cys Val
 1045 1050 1055
 Glu Glu Glu Val Tyr Pro Asn Asn Thr Val Thr Cys Asn Asn Tyr Thr
 1060 1065 1070
 Ala Thr Gln Glu Glu His Glu Gly Thr Tyr Thr Ser Arg Asn Arg Gly
 1075 1080 1085
 Tyr Asp Glu Ala Tyr Glu Ser Asn Ser Ser Val His Ala Ser Val Tyr
 1090 1095 1100
 Glu Glu Lys Ser Tyr Thr Asp Arg Arg Arg Glu Asn Pro Cys Glu Ser
 1105 1110 1115 1120
 Asn Arg Gly Tyr Gly Asp Tyr Thr Pro Leu Pro Ala Gly Tyr Val Thr
 1125 1130 1135
 Lys Glu Leu Glu Tyr Phe Pro Glu Thr Asp Lys Val Trp Ile Glu Ile
 1140 1145 1150
 Gly Glu Thr Glu Gly Thr Phe Ile Val Asp Ser Val Glu Leu Leu Leu
 1155 1160 1165
 Met Glu Glu
 1170

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3558 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Hybrid sequence

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 1..3558

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

| | |
|---|-----|
| ATG GAG ATA GTG AAT AAT CAG AAT CAA TGC GTG CCT TAT AAT TGT TTA | 48 |
| Met Glu Ile Val Asn Asn Gln Asn Gln Cys Val Pro Tyr Asn Cys Leu | |
| 1 5 10 15 | |
| AAT AAT CCT GAA AAT GAG ATA TTA GAT ATT GAA AGG TCA AAT AGT ACT | 96 |
| Asn Asn Pro Glu Asn Glu Ile Leu Asp Ile Glu Arg Ser Asn Ser Thr | |
| 20 25 30 | |
| GTA GCA ACA AAC ATC GCC TTG GAG ATT AGT CGT CTG CTC GCT TCC GCA | 144 |
| Val Ala Thr Asn Ile Ala Leu Glu Ile Ser Arg Leu Leu Ala Ser Ala | |
| 35 40 45 | |
| ACT CCA ATA GGG GGG ATT TTA TTA GGA TTG TTT GAT GCA ATA TGG GGG | 192 |
| Thr Pro Ile Gly Gly Ile Leu Leu Gly Leu Phe Asp Ala Ile Trp Gly | |
| 50 55 60 | |
| TCT ATA GGC CCT TCA CAA TGG GAT TTA TTT TTA GAG CAA ATT GAG CTA | 240 |
| Ser Ile Gly Pro Ser Gln Trp Asp Leu Phe Leu Glu Gln Ile Glu Leu | |
| 65 70 75 80 | |
| TTG ATT GAC CAA AAA ATA GAG GAA TTC GCT AGA AAC CAG GCA ATT TCT | 288 |
| Leu Ile Asp Gln Lys Ile Glu Glu Phe Ala Arg Asn Gln Ala Ile Ser | |
| 85 90 95 | |
| AGA TTG GAA GGG ATA AGC AGT CTG TAC GGA ATT TAT ACA GAA GCT TTT | 336 |
| Arg Leu Glu Gly Ile Ser Ser Leu Tyr Gly Ile Tyr Thr Glu Ala Phe | |
| 100 105 110 | |
| AGA GAG TGG GAA GCA GAT CCT ACT AAT CCA GCA TTA AAA GAA GAG ATG | 384 |
| Arg Glu Trp Glu Ala Asp Pro Thr Asn Pro Ala Leu Lys Glu Glu Met | |
| 115 120 125 | |
| CGT ACT CAA TTT AAT GAC ATG AAC AGT ATT CTT GTA ACA GCT ATT CCT | 432 |
| Arg Thr Gln Phe Asn Asp Met Asn Ser Ile Leu Val Thr Ala Ile Pro | |
| 130 135 140 | |

| | |
|---|------|
| CTT TTT TCA GTT CAA AAT TAT CAA GTC CCA TTT TTA TCA GTA TAT GTT | 480 |
| Leu Phe Ser Val Gln Asn Tyr Gln Val Pro Phe Leu Ser Val Tyr Val | |
| 145 150 155 160 | |
| CAA GCT GCA AAT TTA CAT TTA TCG GTT TTG AGA GAT GTT TCA GTG TTT | 528 |
| Gln Ala Ala Asn Leu His Leu Ser Val Leu Arg Asp Val Ser Val Phe | |
| 165 170 175 | |
| GGG CAG GCT TGG GGA TTT GAT ATA GCA ACA ATA AAT AGT CGT TAT AAT | 576 |
| Gly Gln Ala Trp Gly Phe Asp Ile Ala Thr Ile Asn Ser Arg Tyr Asn | |
| 180 185 190 | |
| GAT CTG ACT AGA CTT ATT CCT ATA TAT ACA GAT TAT GCT GTA CGC TGG | 624 |
| Asp Leu Thr Arg Leu Ile Pro Ile Tyr Thr Asp Tyr Ala Val Arg Trp | |
| 195 200 205 | |
| TAC AAT ACG GGA TTA GAT CGC TTA CCA CGA ACT GGT GGG CTG CGA AAC | 672 |
| Tyr Asn Thr Gly Leu Asp Arg Leu Pro Arg Thr Gly Gly Leu Arg Asn | |
| 210 215 220 | |
| TGG GCA AGA TTT AAT CAG TTT AGA AGA GAG TTA ACA ATA TCA GTA TTA | 720 |
| Trp Ala Arg Phe Asn Gln Phe Arg Arg Glu Leu Thr Ile Ser Val Leu | |
| 225 230 235 240 | |
| GAT ATT ATT TCT TTT TTC AGA AAT TAC GAT TCT AGA TTA TAT CCA ATT | 768 |
| Asp Ile Ile Ser Phe Phe Arg Asn Tyr Asp Ser Arg Leu Tyr Pro Ile | |
| 245 250 255 | |
| CCA ACA AGC TCC CAA TTA ACG CGG GAA GTA TAT ACA GAT CCG GTA ATT | 816 |
| Pro Thr Ser Ser Gln Leu Thr Arg Glu Val Tyr Thr Asp Pro Val Ile | |
| 260 265 270 | |
| AAT ATA ACT GAC TAT AGA GTT GGC CCC AGC TTC GAG AAT ATT GAG AAC | 864 |
| Asn Ile Thr Asp Tyr Arg Val Gly Pro Ser Phe Glu Asn Ile Glu Asn | |
| 275 280 285 | |
| TCA GCC ATT AGA AGC CCC CAC CTT ATG GAC TTC TTA AAT AAT TTG ACC | 912 |
| Ser Ala Ile Arg Ser Pro His Leu Met Asp Phe Leu Asn Asn Leu Thr | |
| 290 295 300 | |
| ATT GAT ACG GAT TTG ATT AGA GGT GTT CAC TAT TGG GCA GGG CAT CGT | 960 |
| Ile Asp Thr Asp Leu Ile Arg Gly Val His Tyr Trp Ala Gly His Arg | |
| 305 310 315 320 | |
| GTA ACT TCT CAT TTT ACA GGT AGT TCT CAA GTG ATA ACA ACC CCT CAA | 1008 |
| Val Thr Ser His Phe Thr Gly Ser Ser Gln Val Ile Thr Thr Pro Gln | |
| 325 330 335 | |
| TAT GGG ATA ACC GCA AAT GCG GAA CCA AGA CGA ACT ATT GCT CCT AGT | 1056 |
| Tyr Gly Ile Thr Ala Asn Ala Glu Pro Arg Arg Thr Ile Ala Pro Ser | |
| 340 345 350 | |

| | |
|---|------|
| ACT TTT CCA GGT CTT AAC CTA TTT TAT AGA ACA TTA TCA AAT CCT TTC | 1104 |
| Thr Phe Pro Gly Leu Asn Leu Phe Tyr Arg Thr Leu Ser Asn Pro Phe | |
| 355 360 365 | |
| TTC CGA AGA TCA GAA AAT ATT ACT CCT ACC TTA GGG ATA AAT GTA GTA | 1152 |
| Phe Arg Arg Ser Glu Asn Ile Thr Pro Thr Leu Gly Ile Asn Val Val | |
| 370 375 380 | |
| CAG GGA GTA GGG TTC ATT CAA CCA AAT AAT GCT GAA GTT CTA TAT AGA | 1200 |
| Gln Gly Val Gly Phe Ile Gln Pro Asn Asn Ala Glu Val Leu Tyr Arg | |
| 385 390 395 400 | |
| AGT AGG GGG ACA GTA GAT TCT CTT AAT GAG TTA CCA ATT GAT GGT GAG | 1248 |
| Ser Arg Gly Thr Val Asp Ser Leu Asn Glu Leu Pro Ile Asp Gly Glu | |
| 405 410 415 | |
| AAT TCA TTA GTT GGA TAT AGT CAT CGA TTA AGT CAT GTT ACA CTA ACC | 1296 |
| Asn Ser Leu Val Gly Tyr Ser His Arg Leu Ser His Val Thr Leu Thr | |
| 420 425 430 | |
| AGG TCG TTA TAT AAT ACT AAT ATA ACT AGC CTG CCA ACA TTT GTT TGG | 1344 |
| Arg Ser Leu Tyr Asn Thr Asn Ile Thr Ser Leu Pro Thr Phe Val Trp | |
| 435 440 445 | |
| ACA CAT CAC AGT GCT ACT AAT ACA AAT ACA ATT AAT CCA GAT ATT ATT | 1392 |
| Thr His His Ser Ala Thr Asn Thr Asn Thr Ile Asn Pro Asp Ile Ile | |
| 450 455 460 | |
| ACA CAA ATA CCT TTA GTG AAA GGA TTT AGA GTT TGG GGG GGC ACC TCT | 1440 |
| Thr Gln Ile Pro Leu Val Lys Gly Phe Arg Val Trp Gly Gly Thr Ser | |
| 465 470 475 480 | |
| GTC ATT ACA GGA CCA GGA TTT ACA GGA GGG GAT ATC CTT CGA AGA AAT | 1488 |
| Val Ile Thr Gly Pro Gly Phe Thr Gly Gly Asp Ile Leu Arg Arg Asn | |
| 485 490 495 | |
| ACC TTT GGT GAT TTT GTA TCT CTA CAA GTC AAT ATT AAT TCA CCA ATT | 1536 |
| Thr Phe Gly Asp Phe Val Ser Leu Gln Val Asn Ile Asn Ser Pro Ile | |
| 500 505 510 | |
| ACC CAA AGA TAC CGT TTA AGA TTT CGT TAC GCT TCC AGT AGG GAT GCA | 1584 |
| Thr Gln Arg Tyr Arg Leu Arg Phe Arg Tyr Ala Ser Ser Arg Asp Ala | |
| 515 520 525 | |
| CGA GTT ATA GTA TTA ACA GGA GCG GCA TCC ACA GGA GTG GGA GGC CAA | 1632 |
| Arg Val Ile Val Leu Thr Gly Ala Ala Ser Thr Gly Val Gly Gly Gln | |
| 530 535 540 | |
| GTT AGT GTA AAT ATG CCT CTT CAG AAA ACT ATG GAA ATA GGG GAG AAC | 1680 |
| Val Ser Val Asn Met Pro Leu Gln Lys Thr Met Glu Ile Gly Glu Asn | |
| 545 550 555 560 | |
| TTA ACA TCT AGA ACA TTT AGA TAT ACC GAT TTT AGT AAT CCT TTT TCA | 1728 |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| Leu | Thr | Ser | Arg | Thr | Phe | Arg | Tyr | Thr | Asp | Phe | Ser | Asn | Pro | Phe | Ser | |
| | | | | 565 | | | | | 570 | | | | | 575 | | |
| TTT | AGA | GCT | AAT | CCA | GAT | ATA | ATT | GGG | ATA | AGT | GAA | CAA | CCT | CTA | TTT | 1776 |
| Phe | Arg | Ala | Asn | Pro | Asp | Ile | Ile | Gly | Ile | Ser | Glu | Gln | Pro | Leu | Phe | |
| | | | 580 | | | | | 585 | | | | 590 | | | | |
| GGT | GCA | GGT | TCT | ATT | AGT | AGC | GGT | GAA | CTT | TAT | ATA | GAT | AAA | ATT | GAA | 1824 |
| Gly | Ala | Gly | Ser | Ile | Ser | Ser | Gly | Glu | Leu | Tyr | Ile | Asp | Lys | Ile | Glu | |
| | | 595 | | | | | 600 | | | | 605 | | | | | |
| ATT | ATT | CTA | GCA | GAT | GCA | ACA | TTT | GAA | GCA | GAA | TCT | GAT | TTA | GAA | AGA | 1872 |
| Ile | Ile | Leu | Ala | Asp | Ala | Thr | Phe | Glu | Ala | Glu | Ser | Asp | Leu | Glu | Arg | |
| | 610 | | | | | 615 | | | | 620 | | | | | | |
| GCA | CAA | AAG | GCG | GTG | AAT | GCC | CTG | TTT | ACT | TCT | TCC | AAT | CAA | ATC | GGG | 1920 |
| Ala | Gln | Lys | Ala | Val | Asn | Ala | Leu | Phe | Thr | Ser | Ser | Asn | Gln | Ile | Gly | |
| 625 | | | | | 630 | | | | 635 | | | | | 640 | | |
| TTA | AAA | ACC | GAT | GTG | ACG | GAT | TAT | CAT | ATT | GAT | CAA | GTA | TCC | AAT | TTA | 1968 |
| Leu | Lys | Thr | Asp | Val | Thr | Asp | Tyr | His | Ile | Asp | Gln | Val | Ser | Asn | Leu | |
| | | | | 645 | | | | 650 | | | | 655 | | | | |
| GTG | GAT | TGT | TTA | TCA | GAT | GAA | TTT | TGT | CTG | GAT | GAA | AAG | CGA | GAA | TTG | 2016 |
| Val | Asp | Cys | Leu | Ser | Asp | Glu | Phe | Cys | Leu | Asp | Glu | Lys | Arg | Glu | Leu | |
| | | | 660 | | | | | 665 | | | | 670 | | | | |
| TCC | GAG | AAA | GTC | AAA | CAT | GCG | AAG | CGA | CTC | AGT | GAT | GAG | CGG | AAT | TTA | 2064 |
| Ser | Glu | Lys | Val | Lys | His | Ala | Lys | Arg | Leu | Ser | Asp | Glu | Arg | Asn | Leu | |
| | | 675 | | | | 680 | | | | | | 685 | | | | |
| CTT | CAA | GAT | CCA | AAC | TTC | AGA | GGG | ATC | AAT | AGA | CAA | CCA | GAC | CGT | GGC | 2112 |
| Leu | Gln | Asp | Pro | Asn | Phe | Arg | Gly | Ile | Asn | Arg | Gln | Pro | Asp | Arg | Gly | |
| | 690 | | | | | 695 | | | | 700 | | | | | | |
| TGG | AGA | GGA | AGT | ACA | GAT | ATT | ACC | ATC | CAA | GGA | GGA | GAT | GAC | GTA | TTC | 2160 |
| Trp | Arg | Gly | Ser | Thr | Asp | Ile | Thr | Ile | Gln | Gly | Gly | Asp | Asp | Val | Phe | |
| 705 | | | | | 710 | | | | 715 | | | | | 720 | | |
| AAA | GAG | AAT | TAC | GTC | ACA | CTA | CCG | GGT | ACC | GTT | GAT | GAG | TGC | TAT | CCA | 2208 |
| Lys | Glu | Asn | Tyr | Val | Thr | Leu | Pro | Gly | Thr | Val | Asp | Glu | Cys | Tyr | Pro | |
| | | | 725 | | | | | 730 | | | | 735 | | | | |
| ACG | TAT | TTA | TAT | CAG | AAA | ATA | GAT | GAG | TCG | AAA | TTA | AAA | GCT | TAT | ACC | 2256 |
| Thr | Tyr | Leu | Tyr | Gln | Lys | Ile | Asp | Glu | Ser | Lys | Leu | Lys | Ala | Tyr | Thr | |
| | | 740 | | | | | | 745 | | | | 750 | | | | |
| CGT | TAT | GAA | TTA | AGA | GGG | TAT | ATC | GAA | GAT | AGT | CAA | GAC | TTA | GAA | ATC | 2304 |
| Arg | Tyr | Glu | Leu | Arg | Gly | Tyr | Ile | Glu | Asp | Ser | Gln | Asp | Leu | Glu | Ile | |
| | | 755 | | | | | 760 | | | | | 765 | | | | |
| TAT | TTG | ATC | CGT | TAC | AAT | GCA | AAA | CAC | GAA | ATA | GTA | AAT | GTG | CCA | GGC | 2352 |
| Tyr | Leu | Ile | Arg | Tyr | Asn | Ala | Lys | His | Glu | Ile | Val | Asn | Val | Pro | Gly | |

| 770 | 775 | 780 | |
|---|-----|-----|------|
| ACG GGT TCC TTA TGG CCG CTT TCA GCC CAA AGT CCA ATC GGA AAG TGT | | | 2400 |
| Thr Gly Ser Leu Trp Pro Leu Ser Ala Gln Ser Pro Ile Gly Lys Cys | | | |
| 785 | 790 | 795 | 800 |
| GGA GAA CCG AAT CGA TGC GCG CCA CAC CTT GAA TGG AAT CCT GAT CTA | | | 2448 |
| Gly Glu Pro Asn Arg Cys Ala Pro His Leu Glu Trp Asn Pro Asp Leu | | | |
| | 805 | 810 | 815 |
| GAT TGT TCC TGC AGA GAC GGG GAA AAA TGT GCA CAT CAT TCC CAT CAT | | | 2496 |
| Asp Cys Ser Cys Arg Asp Gly Glu Lys Cys Ala His His Ser His His | | | |
| | 820 | 825 | 830 |
| TTC ACC TTG GAT ATT GAT GTT GGA TGT ACA GAC TTA AAT GAG GAC TTA | | | 2544 |
| Phe Thr Leu Asp Ile Asp Val Gly Cys Thr Asp Leu Asn Glu Asp Leu | | | |
| | 835 | 840 | 845 |
| GGT GTA TGG GTG ATA TTC AAG ATT AAG ACG CAA GAT GGC CAT GCA AGA | | | 2592 |
| Gly Val Trp Val Ile Phe Lys Ile Lys Thr Gln Asp Gly His Ala Arg | | | |
| | 850 | 855 | 860 |
| CTA GGG AAT CTA GAG TTT CTC GAA GAG AAA CCA TTA TTA GGG GAA GCA | | | 2640 |
| Leu Gly Asn Leu Glu Phe Leu Glu Glu Lys Pro Leu Leu Gly Glu Ala | | | |
| | 865 | 870 | 880 |
| CTA GCT CGT GTG AAA AGA GCG GAG AAG AAG TGG AGA GAC AAA CGA GAG | | | 2688 |
| Leu Ala Arg Val Lys Arg Ala Glu Lys Lys Trp Arg Asp Lys Arg Glu | | | |
| | 885 | 890 | 895 |
| AAA CTG CAG TTG GAA ACA AAT ATT GTT TAT AAA GAG GCA AAA GAA TCT | | | 2736 |
| Lys Leu Gln Leu Glu Thr Asn Ile Val Tyr Lys Glu Ala Lys Glu Ser | | | |
| | 900 | 905 | 910 |
| GTA GAT GCT TTA TTT GTA AAC TCT CAA TAT GAT AGA TTA CAA GTG GAT | | | 2784 |
| Val Asp Ala Leu Phe Val Asn Ser Gln Tyr Asp Arg Leu Gln Val Asp | | | |
| | 915 | 920 | 925 |
| ACG AAC ATC GCG ATG ATT CAT GCG GCA GAT AAA CGC GTT CAT AGA ATC | | | 2832 |
| Thr Asn Ile Ala Met Ile His Ala Ala Asp Lys Arg Val His Arg Ile | | | |
| | 930 | 935 | 940 |
| CGG GAA GCG TAT CTG CCA GAG TTG TCT GTG ATT CCA GGT GTC AAT GCG | | | 2880 |
| Arg Glu Ala Tyr Leu Pro Glu Leu Ser Val Ile Pro Gly Val Asn Ala | | | |
| | 945 | 950 | 955 |
| GCC ATT TTC GAA GAA TTA GAG GGA CGT ATT TTT ACA GCG TAT TCC TTA | | | 2928 |
| Ala Ile Phe Glu Glu Leu Glu Gly Arg Ile Phe Thr Ala Tyr Ser Leu | | | |
| | 965 | 970 | 975 |
| TAT GAT GCG AGA AAT GTC ATT AAA AAT GGC GAT TTC AAT AAT GGC TTA | | | 2976 |
| Tyr Asp Ala Arg Asn Val Ile Lys Asn Gly Asp Phe Asn Asn Gly Leu | | | |
| | 980 | 985 | 990 |

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|---|------|
| TTA TGC TGG AAC GTG AAA GGT CAT GTA GAT GTA GAA GAG CAA AAC AAC Leu Cys Trp Asn Val Lys Gly His Val Asp Val Glu Glu Gln Asn Asn 995 1000 1005 | 3024 |
| CAC CGT TCG GTC CTT GTT ATC CCA GAA TGG GAG GCA GAA GTG TCA CAA His Arg Ser Val Leu Val Ile Pro Glu Trp Glu Ala Glu Val Ser Gln 1010 1015 1020 | 3072 |
| GAG GTT CGT GTC TGT CCA GGT CGT GGC TAT ATC CTT CGT GTC ACA GCA Glu Val Arg Val Cys Pro Gly Arg Gly Tyr Ile Leu Arg Val Thr Ala 1025 1030 1035 1040 | 3120 |
| TAT AAA GAG GGA TAT GGA GAG GGC TGC GTA ACG ATC CAT GAG ATC GAA Tyr Lys Glu Gly Tyr Gly Glu Gly Cys Val Thr Ile His Glu Ile Glu 1045 1050 1055 | 3168 |
| GAC AAT ACA GAC GAA CTG AAA TTC AGC AAC TGT GTA GAA GAG GAA GTA Asp Asn Thr Asp Glu Leu Lys Phe Ser Asn Cys Val Glu Glu Glu Val 1060 1065 1070 | 3216 |
| TAT CCA AAC AAC ACA GTA ACG TGT AAT AAT TAT ACT GGG ACT CAA GAA Tyr Pro Asn Asn Thr Val Thr Cys Asn Asn Tyr Thr Gly Thr Gln Glu 1075 1080 1085 | 3264 |
| GAA TAT GAG GGT ACG TAC ACT TCT CGT AAT CAA GGA TAT GAC GAA GCC Glu Tyr Glu Gly Thr Tyr Thr Ser Arg Asn Gln Gly Tyr Asp Glu Ala 1090 1095 1100 | 3312 |
| TAT GGT AAT AAC CCT TCC GTA CCA GCT GAT TAC GCT TCA GTC TAT GAA Tyr Gly Asn Asn Pro Ser Val Pro Ala Asp Tyr Ala Ser Val Tyr Glu 1105 1110 1115 1120 | 3360 |
| GAA AAA TCG TAT ACA GAT GGA CGA AGA GAG AAT CCT TGT GAA TCT AAC Glu Lys Ser Tyr Thr Asp Gly Arg Arg Glu Asn Pro Cys Glu Ser Asn 1125 1130 1135 | 3408 |
| AGA GGC TAT GGG GAT TAC ACA CCA CTA CCG GCT GGT TAT GTA ACA AAG Arg Gly Tyr Gly Asp Tyr Thr Pro Leu Pro Ala Gly Tyr Val Thr Lys 1140 1145 1150 | 3456 |
| GAT TTA GAG TAC TTC CCA GAG ACC GAT AAG GTA TGG ATT GAG ATC GGA Asp Leu Glu Tyr Phe Pro Glu Thr Asp Lys Val Trp Ile Glu Ile Gly 1155 1160 1165 | 3504 |
| GAA ACA GAA GGA ACA TTC ATC GTG GAT AGC GTG GAA TTA CTC CTT ATG Glu Thr Glu Gly Thr Phe Ile Val Asp Ser Val Glu Leu Leu Met 1170 1175 1180 | 3552 |
| GAG GAA Glu Glu 1185 | 3558 |

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1186 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

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Met Glu Ile Val Asn Asn Gln Asn Gln Cys Val Pro Tyr Asn Cys Leu
 1             5             10             15

Asn Asn Pro Glu Asn Glu Ile Leu Asp Ile Glu Arg Ser Asn Ser Thr
      20             25             30

Val Ala Thr Asn Ile Ala Leu Glu Ile Ser Arg Leu Leu Ala Ser Ala
      35             40             45

Thr Pro Ile Gly Gly Ile Leu Leu Gly Leu Phe Asp Ala Ile Trp Gly
      50             55             60

Ser Ile Gly Pro Ser Gln Trp Asp Leu Phe Leu Glu Gln Ile Glu Leu
      65             70             75             80

Leu Ile Asp Gln Lys Ile Glu Glu Phe Ala Arg Asn Gln Ala Ile Ser
      85             90             95

Arg Leu Glu Gly Ile Ser Ser Leu Tyr Gly Ile Tyr Thr Glu Ala Phe
      100            105            110

Arg Glu Trp Glu Ala Asp Pro Thr Asn Pro Ala Leu Lys Glu Glu Met
      115            120            125

Arg Thr Gln Phe Asn Asp Met Asn Ser Ile Leu Val Thr Ala Ile Pro
      130            135            140

Leu Phe Ser Val Gln Asn Tyr Gln Val Pro Phe Leu Ser Val Tyr Val
      145            150            155            160

Gln Ala Ala Asn Leu His Leu Ser Val Leu Arg Asp Val Ser Val Phe
      165            170            175

Gly Gln Ala Trp Gly Phe Asp Ile Ala Thr Ile Asn Ser Arg Tyr Asn
      180            185            190

Asp Leu Thr Arg Leu Ile Pro Ile Tyr Thr Asp Tyr Ala Val Arg Trp
      195            200            205

Tyr Asn Thr Gly Leu Asp Arg Leu Pro Arg Thr Gly Gly Leu Arg Asn
      210            215            220

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Trp Ala Arg Phe Asn Gln Phe Arg Arg Glu Leu Thr Ile Ser Val Leu
 225 230 235 240
 Asp Ile Ile Ser Phe Phe Arg Asn Tyr Asp Ser Arg Leu Tyr Pro Ile
 245 250 255
 Pro Thr Ser Ser Gln Leu Thr Arg Glu Val Tyr Thr Asp Pro Val Ile
 260 265 270
 Asn Ile Thr Asp Tyr Arg Val Gly Pro Ser Phe Glu Asn Ile Glu Asn
 275 280 285
 Ser Ala Ile Arg Ser Pro His Leu Met Asp Phe Leu Asn Asn Leu Thr
 290 295 300
 Ile Asp Thr Asp Leu Ile Arg Gly Val His Tyr Trp Ala Gly His Arg
 305 310 315 320
 Val Thr Ser His Phe Thr Gly Ser Ser Gln Val Ile Thr Thr Pro Gln
 325 330 335
 Tyr Gly Ile Thr Ala Asn Ala Glu Pro Arg Arg Thr Ile Ala Pro Ser
 340 345 350
 Thr Phe Pro Gly Leu Asn Leu Phe Tyr Arg Thr Leu Ser Asn Pro Phe
 355 360 365
 Phe Arg Arg Ser Glu Asn Ile Thr Pro Thr Leu Gly Ile Asn Val Val
 370 375 380
 Gln Gly Val Gly Phe Ile Gln Pro Asn Asn Ala Glu Val Leu Tyr Arg
 385 390 395 400
 Ser Arg Gly Thr Val Asp Ser Leu Asn Glu Leu Pro Ile Asp Gly Glu
 405 410 415
 Asn Ser Leu Val Gly Tyr Ser His Arg Leu Ser His Val Thr Leu Thr
 420 425 430
 Arg Ser Leu Tyr Asn Thr Asn Ile Thr Ser Leu Pro Thr Phe Val Trp
 435 440 445
 Thr His His Ser Ala Thr Asn Thr Asn Thr Ile Asn Pro Asp Ile Ile
 450 455 460
 Thr Gln Ile Pro Leu Val Lys Gly Phe Arg Val Trp Gly Gly Thr Ser
 465 470 475 480
 Val Ile Thr Gly Pro Gly Phe Thr Gly Gly Asp Ile Leu Arg Arg Asn
 485 490 495
 Thr Phe Gly Asp Phe Val Ser Leu Gln Val Asn Ile Asn Ser Pro Ile

500 505 510
 Thr Gln Arg Tyr Arg Leu Arg Phe Arg Tyr Ala Ser Ser Arg Asp Ala
 515 520 525
 Arg Val Ile Val Leu Thr Gly Ala Ala Ser Thr Gly Val Gly Gly Gln
 530 535 540
 Val Ser Val Asn Met Pro Leu Gln Lys Thr Met Glu Ile Gly Glu Asn
 545 550 555 560
 Leu Thr Ser Arg Thr Phe Arg Tyr Thr Asp Phe Ser Asn Pro Phe Ser
 565 570 575
 Phe Arg Ala Asn Pro Asp Ile Ile Gly Ile Ser Glu Gln Pro Leu Phe
 580 585 590
 Gly Ala Gly Ser Ile Ser Ser Gly Glu Leu Tyr Ile Asp Lys Ile Glu
 595 600 605
 Ile Ile Leu Ala Asp Ala Thr Phe Glu Ala Glu Ser Asp Leu Glu Arg
 610 615 620
 Ala Gln Lys Ala Val Asn Ala Leu Phe Thr Ser Ser Asn Gln Ile Gly
 625 630 635 640
 Leu Lys Thr Asp Val Thr Asp Tyr His Ile Asp Gln Val Ser Asn Leu
 645 650 655
 Val Asp Cys Leu Ser Asp Glu Phe Cys Leu Asp Glu Lys Arg Glu Leu
 660 665 670
 Ser Glu Lys Val Lys His Ala Lys Arg Leu Ser Asp Glu Arg Asn Leu
 675 680 685
 Leu Gln Asp Pro Asn Phe Arg Gly Ile Asn Arg Gln Pro Asp Arg Gly
 690 695 700
 Trp Arg Gly Ser Thr Asp Ile Thr Ile Gln Gly Gly Asp Asp Val Phe
 705 710 715 720
 Lys Glu Asn Tyr Val Thr Leu Pro Gly Thr Val Asp Glu Cys Tyr Pro
 725 730 735
 Thr Tyr Leu Tyr Gln Lys Ile Asp Glu Ser Lys Leu Lys Ala Tyr Thr
 740 745 750
 Arg Tyr Glu Leu Arg Gly Tyr Ile Glu Asp Ser Gln Asp Leu Glu Ile
 755 760 765
 Tyr Leu Ile Arg Tyr Asn Ala Lys His Glu Ile Val Asn Val Pro Gly
 770 775 780

Thr Gly Ser Leu Trp Pro Leu Ser Ala Gln Ser Pro Ile Gly Lys Cys
 785 790 795 800
 Gly Glu Pro Asn Arg Cys Ala Pro His Leu Glu Trp Asn Pro Asp Leu
 805 810 815
 Asp Cys Ser Cys Arg Asp Gly Glu Lys Cys Ala His His Ser His His
 820 825 830
 Phe Thr Leu Asp Ile Asp Val Gly Cys Thr Asp Leu Asn Glu Asp Leu
 835 840 845
 Gly Val Trp Val Ile Phe Lys Ile Lys Thr Gln Asp Gly His Ala Arg
 850 855 860
 Leu Gly Asn Leu Glu Phe Leu Glu Glu Lys Pro Leu Leu Gly Glu Ala
 865 870 875 880
 Leu Ala Arg Val Lys Arg Ala Glu Lys Lys Trp Arg Asp Lys Arg Glu
 885 890 895
 Lys Leu Gln Leu Glu Thr Asn Ile Val Tyr Lys Glu Ala Lys Glu Ser
 900 905 910
 Val Asp Ala Leu Phe Val Asn Ser Gln Tyr Asp Arg Leu Gln Val Asp
 915 920 925
 Thr Asn Ile Ala Met Ile His Ala Ala Asp Lys Arg Val His Arg Ile
 930 935 940
 Arg Glu Ala Tyr Leu Pro Glu Leu Ser Val Ile Pro Gly Val Asn Ala
 945 950 955 960
 Ala Ile Phe Glu Glu Leu Glu Gly Arg Ile Phe Thr Ala Tyr Ser Leu
 965 970 975
 Tyr Asp Ala Arg Asn Val Ile Lys Asn Gly Asp Phe Asn Asn Gly Leu
 980 985 990
 Leu Cys Trp Asn Val Lys Gly His Val Asp Val Glu Glu Gln Asn Asn
 995 1000 1005
 His Arg Ser Val Leu Val Ile Pro Glu Trp Glu Ala Glu Val Ser Gln
 1010 1015 1020
 Glu Val Arg Val Cys Pro Gly Arg Gly Tyr Ile Leu Arg Val Thr Ala
 1025 1030 1035 1040
 Tyr Lys Glu Gly Tyr Gly Glu Gly Cys Val Thr Ile His Glu Ile Glu
 1045 1050 1055
 Asp Asn Thr Asp Glu Leu Lys Phe Ser Asn Cys Val Glu Glu Glu Val
 1060 1065 1070

Tyr Pro Asn Asn Thr Val Thr Cys Asn Asn Tyr Thr Gly Thr Gln Glu
 1075 1080 1085
 Glu Tyr Glu Gly Thr Tyr Thr Ser Arg Asn Gln Gly Tyr Asp Glu Ala
 1090 1095 1100
 Tyr Gly Asn Asn Pro Ser Val Pro Ala Asp Tyr Ala Ser Val Tyr Glu
 1105 1110 1115 1120
 Glu Lys Ser Tyr Thr Asp Gly Arg Arg Glu Asn Pro Cys Glu Ser Asn
 1125 1130 1135
 Arg Gly Tyr Gly Asp Tyr Thr Pro Leu Pro Ala Gly Tyr Val Thr Lys
 1140 1145 1150
 Asp Leu Glu Tyr Phe Pro Glu Thr Asp Lys Val Trp Ile Glu Ile Gly
 1155 1160 1165
 Glu Thr Glu Gly Thr Phe Ile Val Asp Ser Val Glu Leu Leu Leu Met
 1170 1175 1180
 Glu Glu
 1185

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3579 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Hybrid toxin

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..3579

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

ATG GAT AAC AAT CCG AAC ATC AAT GAA TGC ATT CCT TAT AAT TGT TTA
 Met Asp Asn Asn Pro Asn Ile Asn Glu Cys Ile Pro Tyr Asn Cys Leu
 1 5 10 15

48

| | |
|---|-----|
| AGT AAC CCT GAA GTA GAA GTA TTA GGT GGA GAA AGA ATA GAA ACT GGT Ser Asn Pro Glu Val Glu Val Leu Gly Gly Glu Arg Ile Glu Thr Gly 20 25 30 | 96 |
| TAC ACC CCA ATC GAT ATT TCC TTG TCG CTA ACG CAA TTT CTT TTG AGT Tyr Thr Pro Ile Asp Ile Ser Leu Ser Leu Thr Gln Phe Leu Leu Ser 35 40 45 | 144 |
| GAA TTT GTT CCC GGT GCT GGA TTT GTG TTA GGA CTA GTT GAT ATA ATA Glu Phe Val Pro Gly Ala Gly Phe Val Leu Gly Leu Val Asp Ile Ile 50 55 60 | 192 |
| TGG GGA ATT TTT GGT CCC TCT CAA TGG GAC GCA TTT CTT GTA CAA ATT Trp Gly Ile Phe Gly Pro Ser Gln Trp Asp Ala Phe Leu Val Gln Ile 65 70 75 80 | 240 |
| GAA CAG TTA ATT AAC CAA AGA ATA GAA GAA TTC GCT AGG AAC CAA GCC Glu Gln Leu Ile Asn Gln Arg Ile Glu Glu Phe Ala Arg Asn Gln Ala 85 90 95 | 288 |
| ATT TCT AGA TTA GAA GGA CTA AGC AAT CTT TAT CAA ATT TAC GCA GAA Ile Ser Arg Leu Glu Gly Leu Ser Asn Leu Tyr Gln Ile Tyr Ala Glu 100 105 110 | 336 |
| TCT TTT AGA GAG TGG GAA GCA GAT CCT ACT AAT CCA GCA TTA AGA GAA Ser Phe Arg Glu Trp Glu Ala Asp Pro Thr Asn Pro Ala Leu Arg Glu 115 120 125 | 384 |
| GAG ATG CGT ATT CAA TTC AAT GAC ATG AAC AGT GCC CTT ACA ACC GCT Glu Met Arg Ile Gln Phe Asn Asp Met Asn Ser Ala Leu Thr Thr Ala 130 135 140 | 432 |
| ATT CCT CTT TTT GCA GTT CAA AAT TAT CAA GTT CCT CTT TTA TCA GTA Ile Pro Leu Phe Ala Val Gln Asn Tyr Gln Val Pro Leu Leu Ser Val 145 150 155 160 | 480 |
| TAT GTT CAA GCT GCA AAT TTA CAT TTA TCA GTT TTG AGA GAT GTT TCA Tyr Val Gln Ala Ala Asn Leu His Leu Ser Val Leu Arg Asp Val Ser 165 170 175 | 528 |
| GTG TTT GGA CAA AGG TGG GGA TTT GAT GCC GCG ACT ATC AAT AGT CGT Val Phe Gly Gln Arg Trp Gly Phe Asp Ala Ala Thr Ile Asn Ser Arg 180 185 190 | 576 |
| TAT AAT GAT TTA ACT AGG CTT ATT GGC AAC TAT ACA GAT CAT GCT GTA Tyr Asn Asp Leu Thr Arg Leu Ile Gly Asn Tyr Thr Asp His Ala Val 195 200 205 | 624 |
| CGC TGG TAC AAT ACG GGA TTA GAG CGT GTA TGG GGA CCG GAT TCT AGA Arg Trp Tyr Asn Thr Gly Leu Glu Arg Val Trp Gly Pro Asp Ser Arg 210 215 220 | 672 |
| GAT TGG ATA AGA TAT AAT CAA TTT AGA AGA GAA TTA ACA CTA ACT GTA | 720 |

55

| 435 | 440 | 445 | |
|---|-----|-----|------|
| AGA GCT CCT ATG TTC TCT TGG ATA CAT CGT AGT GCA ACT CTT ACA AAT | | | 1392 |
| Arg Ala Pro Met Phe Ser Trp Ile His Arg Ser Ala Thr Leu Thr Asn | | | |
| 450 | 455 | 460 | |
| ACA ATT GAT CCA GAG AGA ATT AAT CAA ATA CCT TTA GTG AAA GGA TTT | | | 1440 |
| Thr Ile Asp Pro Glu Arg Ile Asn Gln Ile Pro Leu Val Lys Gly Phe | | | |
| 465 | 470 | 475 | 480 |
| AGA GTT TGG GGG GGC ACC TCT GTC ATT ACA GGA CCA GGA TTT ACA GGA | | | 1488 |
| Arg Val Trp Gly Gly Thr Ser Val Ile Thr Gly Pro Gly Phe Thr Gly | | | |
| 485 | 490 | 495 | |
| GGG GAT ATC CTT CGA AGA AAT ACC TTT GGT GAT TTT GTA TCT CTA CAA | | | 1536 |
| Gly Asp Ile Leu Arg Arg Asn Thr Phe Gly Asp Phe Val Ser Leu Gln | | | |
| 500 | 505 | 510 | |
| GTC AAT ATT AAT TCA CCA ATT ACC CAA AGA TAC CGT TTA AGA TTT CGT | | | 1584 |
| Val Asn Ile Asn Ser Pro Ile Thr Gln Arg Tyr Arg Leu Arg Phe Arg | | | |
| 515 | 520 | 525 | |
| TAC GCT TCC AGT AGG GAT GCA CGA GTT ATA GTA TTA ACA GGA GCG GCA | | | 1632 |
| Tyr Ala Ser Ser Arg Asp Ala Arg Val Ile Val Leu Thr Gly Ala Ala | | | |
| 530 | 535 | 540 | |
| TCC ACA GGA GTG GGA GGC CAA GTT AGT GTA AAT ATG CCT CTT CAG AAA | | | 1680 |
| Ser Thr Gly Val Gly Gly Gln Val Ser Val Asn Met Pro Leu Gln Lys | | | |
| 545 | 550 | 555 | 560 |
| ACT ATG GAA ATA GGG GAG AAC TTA ACA TCT AGA ACA TTT AGA TAT ACC | | | 1728 |
| Thr Met Glu Ile Gly Glu Asn Leu Thr Ser Arg Thr Phe Arg Tyr Thr | | | |
| 565 | 570 | 575 | |
| GAT TTT AGT AAT CCT TTT TCA TTT AGA GCT AAT CCA GAT ATA ATT GGG | | | 1776 |
| Asp Phe Ser Asn Pro Phe Ser Phe Arg Ala Asn Pro Asp Ile Ile Gly | | | |
| 580 | 585 | 590 | |
| ATA AGT GAA CAA CCT CTA TTT GGT GCA GGT TCT ATT AGT AGC GGT GAA | | | 1824 |
| Ile Ser Glu Gln Pro Leu Phe Gly Ala Gly Ser Ile Ser Ser Gly Glu | | | |
| 595 | 600 | 605 | |
| CTT TAT ATA GAT AAA ATT GAA ATT ATT CTA GCA GAT GCA ACA TTT GAA | | | 1872 |
| Leu Tyr Ile Asp Lys Ile Glu Ile Ile Leu Ala Asp Ala Thr Phe Glu | | | |
| 610 | 615 | 620 | |
| GCA GAA TCT GAT TTA GAA AGA GCA CAA AAG GCG GTG AAT GCC CTG TTT | | | 1920 |
| Ala Glu Ser Asp Leu Glu Arg Ala Gln Lys Ala Val Asn Ala Leu Phe | | | |
| 625 | 630 | 635 | 640 |
| ACT TCT TCC AAT CAA ATC GGG TTA AAA ACC GAT GTG ACG GAT TAT CAT | | | 1968 |
| Thr Ser Ser Asn Gln Ile Gly Leu Lys Thr Asp Val Thr Asp Tyr His | | | |
| 645 | 650 | 655 | |

| | |
|---|------|
| ATT GAT CAA GTA TCC AAT TTA GTG GAT TGT TTA TCA GAT GAA TTT TGT Ile Asp Gln Val Ser Asn Leu Val Asp Cys Leu Ser Asp Glu Phe Cys 660 665 670 | 2016 |
| CTG GAT GAA AAG CGA GAA TTG TCC GAG AAA GTC AAA CAT GCG AAG CGA Leu Asp Glu Lys Arg Glu Leu Ser Glu Lys Val Lys His Ala Lys Arg 675 680 685 | 2064 |
| CTC AGT GAT GAG CGG AAT TTA CTT CAA GAT CCA AAC TTC AGA GGG ATC Leu Ser Asp Glu Arg Asn Leu Leu Gln Asp Pro Asn Phe Arg Gly Ile 690 695 700 | 2112 |
| AAT AGA CAA CCA GAC CGT GGC TGG AGA GGA AGT ACA GAT ATT ACC ATC Asn Arg Gln Pro Asp Arg Gly Trp Arg Gly Ser Thr Asp Ile Thr Ile 705 710 715 720 | 2160 |
| CAA GGA GGA GAT GAC GTA TTC AAA GAG AAT TAC GTC ACA CTA CCG GGT Gln Gly Gly Asp Val Phe Lys Glu Asn Tyr Val Thr Leu Pro Gly 725 730 735 | 2208 |
| ACC GTT GAT GAG TGC TAT CCA ACG TAT TTA TAT CAG AAA ATA GAT GAG Thr Val Asp Glu Cys Tyr Pro Thr Tyr Leu Tyr Gln Lys Ile Asp Glu 740 745 750 | 2256 |
| TCG AAA TTA AAA GCT TAT ACC CGT TAT GAA TTA AGA GGG TAT ATC GAA Ser Lys Leu Lys Ala Tyr Thr Arg Tyr Glu Leu Arg Gly Tyr Ile Glu 755 760 765 | 2304 |
| GAT AGT CAA GAC TTA GAA ATC TAT TTG ATC CGT TAC AAT GCA AAA CAC Asp Ser Gln Asp Leu Glu Ile Tyr Leu Ile Arg Tyr Asn Ala Lys His 770 775 780 | 2352 |
| GAA ATA GTA AAT GTG CCA GGC ACG GGT TCC TTA TGG CCG CTT TCA GCC Glu Ile Val Asn Val Pro Gly Thr Gly Ser Leu Trp Pro Leu Ser Ala 785 790 795 800 | 2400 |
| CAA AGT CCA ATC GGA AAG TGT GGA GAA CCG AAT CGA TGC GCG CCA CAC Gln Ser Pro Ile Gly Lys Cys Gly Glu Pro Asn Arg Cys Ala Pro His 805 810 815 | 2448 |
| CTT GAA TGG AAT CCT GAT CTA GAT TGT TCC TGC AGA GAC GGG GAA AAA Leu Glu Trp Asn Pro Asp Leu Asp Cys Ser Cys Arg Asp Gly Glu Lys 820 825 830 | 2496 |
| TGT GCA CAT CAT TCC CAT CAT TTC ACC TTG GAT ATT GAT GTT GGA TGT Cys Ala His His Ser His His Phe Thr Leu Asp Ile Asp Val Gly Cys 835 840 845 | 2544 |
| ACA GAC TTA AAT GAG GAC TTA GGT GTA TGG GTG ATA TTC AAG ATT AAG Thr Asp Leu Asn Glu Asp Leu Gly Val Trp Val Ile Phe Lys Ile Lys 850 855 860 | 2592 |

ACG CAA GAT GGC CAT GCA AGA CTA GGG AAT CTA GAG TTT CTC GAA GAG 2640
 Thr Gln Asp Gly His Ala Arg Leu Gly Asn Leu Glu Phe Leu Glu Glu
 865 870 875 880

AAA CCA TTA TTA GGG GAA GCA CTA GCT CGT GTG AAA AGA GCG GAG AAG 2688
 Lys Pro Leu Leu Gly Glu Ala Leu Ala Arg Val Lys Arg Ala Glu Lys
 885 890 895

AAG TGG AGA GAC AAA CGA GAG AAA CTG CAG TTG GAA ACA AAT ATT GTT 2736
 Lys Trp Arg Asp Lys Arg Glu Lys Leu Gln Leu Glu Thr Asn Ile Val
 900 905 910

TAT AAA GAG GCA AAA GAA TCT GTA GAT GCT TTA TTT GTA AAC TCT CAA 2784
 Tyr Lys Glu Ala Lys Glu Ser Val Asp Ala Leu Phe Val Asn Ser Gln
 915 920 925

TAT GAT AGA TTA CAA GTG GAT ACG AAC ATC GCG ATG ATT CAT GCG GCA 2832
 Tyr Asp Arg Leu Gln Val Asp Thr Asn Ile Ala Met Ile His Ala Ala
 930 935 940

GAT AAA CGC GTT CAT AGA ATC CGG GAA GCG TAT CTG CCA GAG TTG TCT 2880
 Asp Lys Arg Val His Arg Ile Arg Glu Ala Tyr Leu Pro Glu Leu Ser
 945 950 955 960

GTG ATT CCA GGT GTC AAT GCG GCC ATT TTC GAA GAA TTA GAG GGA CGT 2928
 Val Ile Pro Gly Val Asn Ala Ala Ile Phe Glu Glu Leu Glu Gly Arg
 965 970 975

ATT TTT ACA GCG TAT TCC TTA TAT GAT GCG AGA AAT GTC ATT AAA AAT 2976
 Ile Phe Thr Ala Tyr Ser Leu Tyr Asp Ala Arg Asn Val Ile Lys Asn
 980 985 990

GGC GAT TTC AAT AAT GGC TTA TTA TGC TGG AAC GTG AAA GGT CAT GTA 3024
 Gly Asp Phe Asn Asn Gly Leu Leu Cys Trp Asn Val Lys Gly His Val
 995 1000 1005

GAT GTA GAA GAG CAA AAC AAC CAC CGT TCG GTC CTT GTT ATC CCA GAA 3072
 Asp Val Glu Glu Gln Asn Asn His Arg Ser Val Leu Val Ile Pro Glu
 1010 1015 1020

TGG GAG GCA GAA GTG TCA CAA GAG GTT CGT GTC TGT CCA GGT CGT GGC 3120
 Trp Glu Ala Glu Val Ser Gln Glu Val Arg Val Cys Pro Gly Arg Gly
 1025 1030 1035 1040

TAT ATC CTT CGT GTC ACA GCA TAT AAA GAG GGA TAT GGA GAG GGC TGC 3168
 Tyr Ile Leu Arg Val Thr Ala Tyr Lys Glu Gly Tyr Gly Glu Gly Cys
 1045 1050 1055

GTA ACG ATC CAT GAG ATC GAA GAC AAT ACA GAC GAA CTG AAA TTC AGC 3216
 Val Thr Ile His Glu Ile Glu Asp Asn Thr Asp Glu Leu Lys Phe Ser
 1060 , 1065 1070

AAC TGT GTA GAA GAG GAA GTA TAT CCA AAC AAC ACA GTA ACG TGT AAT 3264

Asn Cys Val Glu Glu Glu Val Tyr Pro Asn Asn Thr Val Thr Cys Asn
 1075 1080 1085

AAT TAT ACT GGG ACT CAA GAA GAA TAT GAG GGT ACG TAC ACT TCT CGT 3312
 Asn Tyr Thr Gly Thr Gln Glu Glu Tyr Glu Gly Thr Tyr Thr Ser Arg
 1090 1095 1100

AAT CAA GGA TAT GAC GAA GCC TAT GGT AAT AAC CCT TCC GTA CCA GCT 3360
 Asn Gln Gly Tyr Asp Glu Ala Tyr Gly Asn Asn Pro Ser Val Pro Ala
 1105 1110 1115 1120

GAT TAC GCT TCA GTC TAT GAA GAA AAA TCG TAT ACA GAT GGA CGA AGA 3408
 Asp Tyr Ala Ser Val Tyr Glu Glu Lys Ser Tyr Thr Asp Gly Arg Arg
 1125 1130 1135

GAG AAT CCT TGT GAA TCT AAC AGA GGC TAT GGG GAT TAC ACA CCA CTA 3456
 Glu Asn Pro Cys Glu Ser Asn Arg Gly Tyr Gly Asp Tyr Thr Pro Leu
 1140 1145 1150

CCG GCT GGT TAT GTA ACA AAG GAT TTA GAG TAC TTC CCA GAG ACC GAT 3504
 Pro Ala Gly Tyr Val Thr Lys Asp Leu Glu Tyr Phe Pro Glu Thr Asp
 1155 1160 1165

AAG GTA TGG ATT GAG ATC GGA GAA ACA GAA GGA ACA TTC ATC GTG GAT 3552
 Lys Val Trp Ile Glu Ile Gly Glu Thr Glu Gly Thr Phe Ile Val Asp
 1170 1175 1180

AGC GTG GAA TTA CTC CTT ATG GAG GAA 3579
 Ser Val Glu Leu Leu Leu Met Glu Glu
 1185 1190

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1193 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Asp Asn Asn Pro Asn Ile Asn Glu Cys Ile Pro Tyr Asn Cys Leu
 1 5 10 15

Ser Asn Pro Glu Val Glu Val Leu Gly Gly Glu Arg Ile Glu Thr Gly
 20 25 30

Tyr Thr Pro Ile Asp Ile Ser Leu Ser Leu Thr Gln Phe Leu Leu Ser
 35 40 45

Glu Phe Val Pro Gly Ala Gly Phe Val Leu Gly Leu Val Asp Ile Ile

| 50 | | | | | 55 | | | | | 60 | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Trp | Gly | Ile | Phe | Gly | Pro | Ser | Gln | Trp | Asp | Ala | Phe | Leu | Val | Gln | Ile | |
| 65 | | | | | 70 | | | | | 75 | | | | 80 | | |
| Glu | Gln | Leu | Ile | Asn | Gln | Arg | Ile | Glu | Glu | Phe | Ala | Arg | Asn | Gln | Ala | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| Ile | Ser | Arg | Leu | Glu | Gly | Leu | Ser | Asn | Leu | Tyr | Gln | Ile | Tyr | Ala | Glu | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| Ser | Phe | Arg | Glu | Trp | Glu | Ala | Asp | Pro | Thr | Asn | Pro | Ala | Leu | Arg | Glu | |
| | | | 115 | | | | 120 | | | | | 125 | | | | |
| Glu | Met | Arg | Ile | Gln | Phe | Asn | Asp | Met | Asn | Ser | Ala | Leu | Thr | Thr | Ala | |
| 130 | | | | | | 135 | | | | | 140 | | | | | |
| Ile | Pro | Leu | Phe | Ala | Val | Gln | Asn | Tyr | Gln | Val | Pro | Leu | Leu | Ser | Val | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | |
| Tyr | Val | Gln | Ala | Ala | Asn | Leu | His | Leu | Ser | Val | Leu | Arg | Asp | Val | Ser | |
| | | | 165 | | | | | | 170 | | | | | 175 | | |
| Val | Phe | Gly | Gln | Arg | Trp | Gly | Phe | Asp | Ala | Ala | Thr | Ile | Asn | Ser | Arg | |
| | | | 180 | | | | | 185 | | | | | 190 | | | |
| Tyr | Asn | Asp | Leu | Thr | Arg | Leu | Ile | Gly | Asn | Tyr | Thr | Asp | His | Ala | Val | |
| | | | 195 | | | | 200 | | | | | 205 | | | | |
| Arg | Trp | Tyr | Asn | Thr | Gly | Leu | Glu | Arg | Val | Trp | Gly | Pro | Asp | Ser | Arg | |
| | | | 210 | | | 215 | | | | | 220 | | | | | |
| Asp | Trp | Ile | Arg | Tyr | Asn | Gln | Phe | Arg | Arg | Glu | Leu | Thr | Leu | Thr | Val | |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 | |
| Leu | Asp | Ile | Val | Ser | Leu | Phe | Pro | Asn | Tyr | Asp | Ser | Arg | Thr | Tyr | Pro | |
| | | | | 245 | | | | | 250 | | | | | 255 | | |
| Ile | Arg | Thr | Val | Ser | Gln | Leu | Thr | Arg | Glu | Ile | Tyr | Thr | Asn | Pro | Val | |
| | | | 260 | | | | | 265 | | | | | 270 | | | |
| Leu | Glu | Asn | Phe | Asp | Gly | Ser | Phe | Arg | Gly | Ser | Ala | Gln | Gly | Ile | Glu | |
| | | | 275 | | | | 280 | | | | | 285 | | | | |
| Gly | Ser | Ile | Arg | Ser | Pro | His | Leu | Met | Asp | Ile | Leu | Asn | Ser | Ile | Thr | |
| | | | 290 | | | 295 | | | | | 300 | | | | | |
| Ile | Tyr | Thr | Asp | Ala | His | Arg | Gly | Glu | Tyr | Tyr | Trp | Ser | Gly | His | Gln | |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 | |
| Ile | Met | Ala | Ser | Pro | Val | Gly | Phe | Ser | Gly | Pro | Glu | Phe | Thr | Phe | Pro | |
| | | | | 325 | | | | | 330 | | | | | 335 | | |

Leu Tyr Gly Thr Met Gly Asn Ala Ala Pro Gln Gln Arg Ile Val Ala
 340 345 350
 Gln Leu Gly Gln Gly Val Tyr Arg Thr Leu Ser Ser Thr Leu Tyr Arg
 355 360 365
 Arg Pro Phe Asn Ile Gly Ile Asn Asn Gln Gln Leu Ser Val Leu Asp
 370 375 380
 Gly Thr Glu Phe Ala Tyr Gly Thr Ser Ser Asn Leu Pro Ser Ala Val
 385 390 395 400
 Tyr Arg Lys Ser Gly Thr Val Asp Ser Leu Asp Glu Ile Pro Pro Gln
 405 410 415
 Asn Asn Asn Val Pro Pro Arg Gln Gly Phe Ser His Arg Leu Ser His
 420 425 430
 Val Ser Met Phe Arg Ser Gly Phe Ser Asn Ser Ser Val Ser Ile Ile
 435 440 445
 Arg Ala Pro Met Phe Ser Trp Ile His Arg Ser Ala Thr Leu Thr Asn
 450 455 460
 Thr Ile Asp Pro Glu Arg Ile Asn Gln Ile Pro Leu Val Lys Gly Phe
 465 470 475 480
 Arg Val Trp Gly Gly Thr Ser Val Ile Thr Gly Pro Gly Phe Thr Gly
 485 490 495
 Gly Asp Ile Leu Arg Arg Asn Thr Phe Gly Asp Phe Val Ser Leu Gln
 500 505 510
 Val Asn Ile Asn Ser Pro Ile Thr Gln Arg Tyr Arg Leu Arg Phe Arg
 515 520 525
 Tyr Ala Ser Ser Arg Asp Ala Arg Val Ile Val Leu Thr Gly Ala Ala
 530 535 540
 Ser Thr Gly Val Gly Gly Gln Val Ser Val Asn Met Pro Leu Gln Lys
 545 550 555 560
 Thr Met Glu Ile Gly Glu Asn Leu Thr Ser Arg Thr Phe Arg Tyr Thr
 565 570 575
 Asp Phe Ser Asn Pro Phe Ser Phe Arg Ala Asn Pro Asp Ile Ile Gly
 580 585 590
 Ile Ser Glu Gln Pro Leu Phe Gly Ala Gly Ser Ile Ser Ser Gly Glu
 595 600 605
 Leu Tyr Ile Asp Lys Ile Glu Ile Ile Leu Ala Asp Ala Thr Phe Glu
 610 615 620

Ala Glu Ser Asp Leu Glu Arg Ala Gln Lys Ala Val Asn Ala Leu Phe
 625 630 635 640
 Thr Ser Ser Asn Gln Ile Gly Leu Lys Thr Asp Val Thr Asp Tyr His
 645 650 655
 Ile Asp Gln Val Ser Asn Leu Val Asp Cys Leu Ser Asp Glu Phe Cys
 660 665 670
 Leu Asp Glu Lys Arg Glu Leu Ser Glu Lys Val Lys His Ala Lys Arg
 675 680 685
 Leu Ser Asp Glu Arg Asn Leu Leu Gln Asp Pro Asn Phe Arg Gly Ile
 690 695 700
 Asn Arg Gln Pro Asp Arg Gly Trp Arg Gly Ser Thr Asp Ile Thr Ile
 705 710 715 720
 Gln Gly Gly Asp Asp Val Phe Lys Glu Asn Tyr Val Thr Leu Pro Gly
 725 730 735
 Thr Val Asp Glu Cys Tyr Pro Thr Tyr Leu Tyr Gln Lys Ile Asp Glu
 740 745 750
 Ser Lys Leu Lys Ala Tyr Thr Arg Tyr Glu Leu Arg Gly Tyr Ile Glu
 755 760 765
 Asp Ser Gln Asp Leu Glu Ile Tyr Leu Ile Arg Tyr Asn Ala Lys His
 770 775 780
 Glu Ile Val Asn Val Pro Gly Thr Gly Ser Leu Trp Pro Leu Ser Ala
 785 790 795 800
 Gln Ser Pro Ile Gly Lys Cys Gly Glu Pro Asn Arg Cys Ala Pro His
 805 810 815
 Leu Glu Trp Asn Pro Asp Leu Asp Cys Ser Cys Arg Asp Gly Glu Lys
 820 825 830
 Cys Ala His His Ser His His Phe Thr Leu Asp Ile Asp Val Gly Cys
 835 840 845
 Thr Asp Leu Asn Glu Asp Leu Gly Val Trp Val Ile Phe Lys Ile Lys
 850 855 860
 Thr Gln Asp Gly His Ala Arg Leu Gly Asn Leu Glu Phe Leu Glu Glu
 865 870 875 880
 Lys Pro Leu Leu Gly Glu Ala Leu Ala Arg Val Lys Arg Ala Glu Lys
 885 890 895
 Lys Trp Arg Asp Lys Arg Glu Lys Leu Gln Leu Glu Thr Asn Ile Val

| | | |
|---|------|-----------|
| 900 | 905 | 910 |
| Tyr Lys Glu Ala Lys Glu Ser Val Asp Ala Leu Phe Val Asn Ser Gln 915 | 920 | 925 |
| Tyr Asp Arg Leu Gln Val Asp Thr Asn Ile Ala Met Ile His Ala Ala 930 | 935 | 940 |
| Asp Lys Arg Val His Arg Ile Arg Glu Ala Tyr Leu Pro Glu Leu Ser 945 | 950 | 955 960 |
| Val Ile Pro Gly Val Asn Ala Ala Ile Phe Glu Glu Leu Glu Gly Arg 965 | 970 | 975 |
| Ile Phe Thr Ala Tyr Ser Leu Tyr Asp Ala Arg Asn Val Ile Lys Asn 980 | 985 | 990 |
| Gly Asp Phe Asn Asn Gly Leu Leu Cys Trp Asn Val Lys Gly His Val 995 | 1000 | 1005 |
| Asp Val Glu Glu Gln Asn Asn His Arg Ser Val Leu Val Ile Pro Glu 1010 | 1015 | 1020 |
| Trp Glu Ala Glu Val Ser Gln Glu Val Arg Val Cys Pro Gly Arg Gly 1025 | 1030 | 1035 1040 |
| Tyr Ile Leu Arg Val Thr Ala Tyr Lys Glu Gly Tyr Gly Glu Gly Cys 1045 | 1050 | 1055 |
| Val Thr Ile His Glu Ile Glu Asp Asn Thr Asp Glu Leu Lys Phe Ser 1060 | 1065 | 1070 |
| Asn Cys Val Glu Glu Glu Val Tyr Pro Asn Asn Thr Val Thr Cys Asn 1075 | 1080 | 1085 |
| Asn Tyr Thr Gly Thr Gln Glu Glu Tyr Glu Gly Thr Tyr Thr Ser Arg 1090 | 1095 | 1100 |
| Asn Gln Gly Tyr Asp Glu Ala Tyr Gly Asn Asn Pro Ser Val Pro Ala 1105 | 1110 | 1115 1120 |
| Asp Tyr Ala Ser Val Tyr Glu Glu Lys Ser Tyr Thr Asp Gly Arg Arg 1125 | 1130 | 1135 |
| Glu Asn Pro Cys Glu Ser Asn Arg Gly Tyr Gly Asp Tyr Thr Pro Leu 1140 | 1145 | 1150 |
| Pro Ala Gly Tyr Val Thr Lys Asp Leu Glu Tyr Phe Pro Glu Thr Asp 1155 | 1160 | 1165 |
| Lys Val Trp Ile Glu Ile Gly Glu Thr Glu Gly Thr Phe Ile Val Asp 1170 | 1175 | 1180 |

Ser Val Glu Leu Leu Leu Met Glu Glu
1185 1190

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3468 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: *Bacillus thuringiensis*

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..3468

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

| | |
|---|-----|
| ATG AAT CAA AAT AAA CAC GGA ATT ATT GGC GCT TCC AAT TGT GGT TGT | 48 |
| Met Asn Gln Asn Lys His Gly Ile Ile Gly Ala Ser Asn Cys Gly Cys | |
| 1 5 10 15 | |
| GCA TCT GAT GAT GTT GCG AAA TAT CCT TTA GCC AAC AAT CCA TAT TCA | 96 |
| Ala Ser Asp Asp Val Ala Lys Tyr Pro Leu Ala Asn Asn Pro Tyr Ser | |
| 20 25 30 | |
| TCT GCT TTA AAT TTA AAT TCT TGT CAA AAT AGT AGT ATT CTC AAC TGG | 144 |
| Ser Ala Leu Asn Leu Asn Ser Cys Gln Asn Ser Ser Ile Leu Asn Trp | |
| 35 40 45 | |
| ATT AAC ATA ATA GGC GAT GCA GCA AAA GAA GCA GTA TCT ATT GGG ACA | 192 |
| Ile Asn Ile Ile Gly Asp Ala Ala Lys Glu Ala Val Ser Ile Gly Thr | |
| 50 55 60 | |
| ACC ATA GTC TCT CTT ATC ACA GCA CCT TCT CTT ACT GGA TTA ATT TCA | 240 |
| Thr Ile Val Ser Leu Ile Thr Ala Pro Ser Leu Thr Gly Leu Ile Ser | |
| 65 70 75 80 | |
| ATA GTA TAT GAC CTT ATA GGT AAA GTA CTA GGA GGT AGT AGT GGA CAA | 288 |
| Ile Val Tyr Asp Leu Ile Gly Lys Val Leu Gly Gly Ser Ser Gly Gln | |
| 85 90 95 | |
| TCC ATA TCA GAT TTG TCT ATA TGT GAC TTA TTA TCT ATT ATT GAT TTA | 336 |
| Ser Ile Ser Asp Leu Ser Ile Cys Asp Leu Leu Ser Ile Ile Asp Leu | |
| 100 105 110 | |
| CGG GTA AGT CAG AGT GTT TTA AAT GAT GGG ATT GCA GAT TTT AAT GGT | 384 |

| | |
|---|------|
| Arg Val Ser Gln Ser Val Leu Asn Asp Gly Ile Ala Asp Phe Asn Gly | |
| 115 120 125 | |
| TCT GTA CTC TTA TAC AGG AAC TAT TTA GAG GCT CTG GAT AGC TGG AAT | 432 |
| Ser Val Leu Leu Tyr Arg Asn Tyr Leu Glu Ala Leu Asp Ser Trp Asn | |
| 130 135 140 | |
| AAG AAT CCT AAT TCT GCT TCT GCT GAA GAA CTC CGT ACT CGT TTT AGA | 480 |
| Lys Asn Pro Asn Ser Ala Ser Ala Glu Glu Leu Arg Thr Arg Phe Arg | |
| 145 150 155 160 | |
| ATC GCC GAC TCA GAA TTT GAT AGA ATT TTA ACC CGA GGG TCT TTA ACG | 528 |
| Ile Ala Asp Ser Glu Phe Asp Arg Ile Leu Thr Arg Gly Ser Leu Thr | |
| 165 170 175 | |
| AAT GGT GGC TCG TTA GCT AGA CAA AAT GCC CAA ATA TTA TTA TTA CCT | 576 |
| Asn Gly Gly Ser Leu Ala Arg Gln Asn Ala Gln Ile Leu Leu Leu Pro | |
| 180 185 190 | |
| TCT TTT GCG AGC GCT GCA TTT TTC CAT TTA TTA CTA CTA AGG GAT GCT | 624 |
| Ser Phe Ala Ser Ala Ala Phe Phe His Leu Leu Leu Leu Arg Asp Ala | |
| 195 200 205 | |
| ACT AGA TAT GGC ACT AAT TGG GGG CTA TAC AAT GCT ACA CCT TTT ATA | 672 |
| Thr Arg Tyr Gly Thr Asn Trp Gly Leu Tyr Asn Ala Thr Pro Phe Ile | |
| 210 215 220 | |
| AAT TAT CAA TCA AAA CTA GTA GAG CTT ATT GAA CTA TAT ACT GAT TAT | 720 |
| Asn Tyr Gln Ser Lys Leu Val Glu Leu Ile Glu Leu Tyr Thr Asp Tyr | |
| 225 230 235 240 | |
| TGC GTA CAT TGG TAT AAT CGA GGT TTC AAC GAA CTA AGA CAA CGA GGC | 768 |
| Cys Val His Trp Tyr Asn Arg Gly Phe Asn Glu Leu Arg Gln Arg Gly | |
| 245 250 255 | |
| ACT AGT GCT ACA GCT TGG TTA GAA TTT CAT AGA TAT CGT AGA GAG ATG | 816 |
| Thr Ser Ala Thr Ala Trp Leu Glu Phe His Arg Tyr Arg Arg Glu Met | |
| 260 265 270 | |
| ACA TTG ATG GTA TTA GAT ATA GTA GCA TCA TTT TCA AGT CTT GAT ATT | 864 |
| Thr Leu Met Val Leu Asp Ile Val Ala Ser Phe Ser Ser Leu Asp Ile | |
| 275 280 285 | |
| ACT AAT TAC CCA ATA GAA ACA GAT TTT CAG TTG AGT AGG GTC ATT TAT | 912 |
| Thr Asn Tyr Pro Ile Glu Thr Asp Phe Gln Leu Ser Arg Val Ile Tyr | |
| 290 295 300 | |
| ACA GAT CCA ATT GGT TTT GTA CAT CGT AGT AGT CTT AGG GGA GAA AGT | 960 |
| Thr Asp Pro Ile Gly Phe Val His Arg Ser Ser Leu Arg Gly Glu Ser | |
| 305 310 315 320 | |
| TGG TTT AGC TTT GTT AAT AGA GCT AAT TTC TCA GAT TTA GAA AAT GCA | 1008 |
| Trp Phe Ser Phe Val Asn Arg Ala Asn Phe Ser Asp Leu Glu Asn Ala | |

| 325 | 330 | 335 | |
|---|-----|-----|------|
| ATA CCT AAT CCT AGA CCG TCT TGG TTT TTA AAT AAT ATG ATT ATA TCT | | | 1056 |
| Ile Pro Asn Pro Arg Pro Ser Trp Phe Leu Asn Asn Met Ile Ile Ser | | | |
| 340 | 345 | 350 | |
| ACT GGT TCA CTT ACA TTG CCG GTT AGC CCA AGT ACT GAT AGA GCG AGG | | | 1104 |
| Thr Gly Ser Leu Thr Leu Pro Val Ser Pro Ser Thr Asp Arg Ala Arg | | | |
| 355 | 360 | 365 | |
| GTA TGG TAT GGA AGT CGA GAT CGA ATT TCC CCT GCT AAT TCA CAA TTT | | | 1152 |
| Val Trp Tyr Gly Ser Arg Asp Arg Ile Ser Pro Ala Asn Ser Gln Phe | | | |
| 370 | 375 | 380 | |
| ATT ACT GAA CTA ATC TCT GGA CAA CAT ACG ACT GCT ACA CAA ACT ATT | | | 1200 |
| Ile Thr Glu Leu Ile Ser Gly Gln His Thr Thr Ala Thr Gln Thr Ile | | | |
| 385 | 390 | 395 | 400 |
| TTA GGG CGA AAT ATA TTT AGA GTA GAT TCT CAA GCT TGT AAT TTA AAT | | | 1248 |
| Leu Gly Arg Asn Ile Phe Arg Val Asp Ser Gln Ala Cys Asn Leu Asn | | | |
| 405 | 410 | 415 | |
| GAT ACC ACA TAT GGA GTG AAT AGG GCG GTA TTT TAT CAT GAT GCG AGT | | | 1296 |
| Asp Thr Thr Tyr Gly Val Asn Arg Ala Val Phe Tyr His Asp Ala Ser | | | |
| 420 | 425 | 430 | |
| GAA GGT TCT CAA AGA TCC GTG TAC GAG GGG TAT ATT CGA ACA ACT GGG | | | 1344 |
| Glu Gly Ser Gln Arg Ser Val Tyr Glu Gly Tyr Ile Arg Thr Thr Gly | | | |
| 435 | 440 | 445 | |
| ATA GAT AAC CCT AGA GTT CAA AAT ATT AAC ACT TAT TTA CCT GGA GAA | | | 1392 |
| Ile Asp Asn Pro Arg Val Gln Asn Ile Asn Thr Tyr Leu Pro Gly Glu | | | |
| 450 | 455 | 460 | |
| AAT TCA GAT ATC CCA ACT CCA GAA GAC TAT ACT CAT ATA TTA AGC ACA | | | 1440 |
| Asn Ser Asp Ile Pro Thr Pro Glu Asp Tyr Thr His Ile Leu Ser Thr | | | |
| 465 | 470 | 475 | 480 |
| ACA ATA AAT TTA ACA GGA GGA CTT AGA CAA GTA GCA TCT AAT CGC CGT | | | 1488 |
| Thr Ile Asn Leu Thr Gly Gly Leu Arg Gln Val Ala Ser Asn Arg Arg | | | |
| 485 | 490 | 495 | |
| TCA TCT TTA GTA ATG TAT GGT TGG ACA CAT AAA AGT CTG GCT CGT AAC | | | 1536 |
| Ser Ser Leu Val Met Tyr Gly Trp Thr His Lys Ser Leu Ala Arg Asn | | | |
| 500 | 505 | 510 | |
| AAT ACC ATT AAT CCA GAT AGA ATT ACA CAG ATA CCA TTG ACG AAG GTT | | | 1584 |
| Asn Thr Ile Asn Pro Asp Arg Ile Thr Gln Ile Pro Leu Thr Lys Val | | | |
| 515 | 520 | 525 | |
| GAT ACC CGA GGC ACA GGT GTT TCT TAT GTG AAT GAT CCA GGA TTT ATA | | | 1632 |
| Asp Thr Arg Gly Thr Gly Val Ser Tyr Val Asn Asp Pro Gly Phe Ile | | | |
| 530 | 535 | 540 | |

| | |
|---|------|
| GTT ACT ATT AGT GAG GGC GGG CCA TTC TAT AAA GGC CGT GCA ATT CAG | 2304 |
| Val Thr Ile Ser Glu Gly Gly Pro Phe Tyr Lys Gly Arg Ala Ile Gln | |
| 755 760 765 | |
| CTA GCA AGT GCA CGA GAA AAT TAC CCA ACA TAC ATC TAT CAA AAA GTA | 2352 |
| Leu Ala Ser Ala Arg Glu Asn Tyr Pro Thr Tyr Ile Tyr Gln Lys Val | |
| 770 775 780 | |
| GAT GCA TCG GAG TTA AAG CCG TAT ACA CGT TAT AGA CTG GAT GGG TTC | 2400 |
| Asp Ala Ser Glu Leu Lys Pro Tyr Thr Arg Tyr Arg Leu Asp Gly Phe | |
| 785 790 795 800 | |
| GTG AAG AGT AGT CAA GAT TTA GAA ATT GAT CTC ATT CAC CAT CAT AAA | 2448 |
| Val Lys Ser Ser Gln Asp Leu Glu Ile Asp Leu Ile His His His Lys | |
| 805 810 815 | |
| GTC CAT CTT GTG AAA AAT GTA CCA GAT AAT TTA GTA TCT GAT ACT TAC | 2496 |
| Val His Leu Val Lys Asn Val Pro Asp Asn Leu Val Ser Asp Thr Tyr | |
| 820 825 830 | |
| CCA GAT GAT TCT TGT AGT GGA ATC AAT CGA TGT CAG GAA CAA CAG ATG | 2544 |
| Pro Asp Asp Ser Cys Ser Gly Ile Asn Arg Cys Gln Glu Gln Gln Met | |
| 835 840 845 | |
| GTA AAT GCG CAA CTG GAA ACA GAG CAT CAT CAT CCG ATG GAT TGC TGT | 2592 |
| Val Asn Ala Gln Leu Glu Thr Glu His His His Pro Met Asp Cys Cys | |
| 850 855 860 | |
| GAA GCA GCT CAA ACA CAT GAG TTT TCT TCC TAT ATT GAT ACA GGG GAT | 2640 |
| Glu Ala Ala Gln Thr His Glu Phe Ser Ser Tyr Ile Asp Thr Gly Asp | |
| 865 870 875 880 | |
| TTA AAT TCG AGT GTA GAC CAG GGA ATC TGG GCG ATC TTT AAA GTT CGA | 2688 |
| Leu Asn Ser Ser Val Asp Gln Gly Ile Trp Ala Ile Phe Lys Val Arg | |
| 885 890 895 | |
| ACA ACC GAT GGT TAT GCG ACG TTA GGA AAT CTT GAA TTG GTA GAG GTC | 2736 |
| Thr Thr Asp Gly Tyr Ala Thr Leu Gly Asn Leu Glu Leu Val Glu Val | |
| 900 905 910 | |
| GGA CCG TTA TCG GGT GAA TCT TTA GAA CGT GAA CAA AGG GAT AAT ACA | 2784 |
| Gly Pro Leu Ser Gly Glu Ser Leu Glu Arg Glu Gln Arg Asp Asn Thr | |
| 915 920 925 | |
| AAA TGG AGT GCA GAG CTA GGA AGA AAG CGT GCA GAA ACA GAT CGC GTG | 2832 |
| Lys Trp Ser Ala Glu Leu Gly Arg Lys Arg Ala Glu Thr Asp Arg Val | |
| 930 935 940 | |
| TAT CAA GAT GCC AAA CAA TCC ATC AAT CAT TTA TTT GTG GAT TAT CAA | 2880 |
| Tyr Gln Asp Ala Lys Gln Ser Ile Asn His Leu Phe Val Asp Tyr Gln | |
| 945 950 955 960 | |
| GAT CAA CAA TTA AAT CCA GAA ATA GGG ATG GCA GAT ATT ATG GAC GCT | 2928 |

Asp Gln Gln Leu Asn Pro Glu Ile Gly Met Ala Asp Ile Met Asp Ala
 965 970 975

CAA AAT CTT GTC GCA TCA ATT TCA GAT GTA TAT AGC GAT GCC GTA CTG 2976
 Gln Asn Leu Val Ala Ser Ile Ser Asp Val Tyr Ser Asp Ala Val Leu
 980 985 990

CAA ATC CCT GGA ATT AAC TAT GAG ATT TAC ACA GAG CTG TCC AAT CGC 3024
 Gln Ile Pro Gly Ile Asn Tyr Glu Ile Tyr Thr Glu Leu Ser Asn Arg
 995 1000 1005

TTA CAA CAA GCA TCG TAT CTG TAT ACG TCT CGA AAT GCG GTG CAA AAT 3072
 Leu Gln Gln Ala Ser Tyr Leu Tyr Thr Ser Arg Asn Ala Val Gln Asn
 1010 1015 1020

GGG GAC TTT AAC AAC GGG CTA GAT AGC TGG AAT GCA ACA GCG GGT GCA 3120
 Gly Asp Phe Asn Asn Gly Leu Asp Ser Trp Asn Ala Thr Ala Gly Ala
 1025 1030 1035 1040

TCG GTA CAA CAG GAT GGC AAT ACG CAT TTC TTA GTT CTT TCT CAT TGG 3168
 Ser Val Gln Gln Asp Gly Asn Thr His Phe Leu Val Leu Ser His Trp
 1045 1050 1055

GAT GCA CAA GTT TCT CAA CAA TTT AGA GTG CAG CCG AAT TGT AAA TAT 3216
 Asp Ala Gln Val Ser Gln Gln Phe Arg Val Gln Pro Asn Cys Lys Tyr
 1060 1065 1070

GTA TTA CGT GTA ACA GCA GAG AAA GTA GGC GGC GGA GAC GGA TAC GTG 3264
 Val Leu Arg Val Thr Ala Glu Lys Val Gly Gly Gly Asp Gly Tyr Val
 1075 1080 1085

ACT ATC CGG GAT GAT GCT CAT CAT ACA GAA ACG CTT ACA TTT AAT GCA 3312
 Thr Ile Arg Asp Asp Ala His His Thr Glu Thr Leu Thr Phe Asn Ala
 1090 1095 1100

TGT GAT TAT GAT ATA AAT GGC ACG TAC GTG ACT GAT AAT ACG TAT CTA 3360
 Cys Asp Tyr Asp Ile Asn Gly Thr Tyr Val Thr Asp Asn Thr Tyr Leu
 1105 1110 1115 1120

ACA AAA GAA GTG GTA TTC CAT CCG GAG ACA CAA CAC ATG TGG GTA GAG 3408
 Thr Lys Glu Val Val Phe His Pro Glu Thr Gln His Met Trp Val Glu
 1125 1130 1135

GTA AAT GAA ACA GAA GGT GCA TTT CAT ATA GAT AGT ATT GAA TTC GTT 3456
 Val Asn Glu Thr Glu Gly Ala Phe His Ile Asp Ser Ile Glu Phe Val
 1140 1145 1150

GAA ACA GAA AAG 3468
 Glu Thr Glu Lys
 1155

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1156 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

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Met Asn Gln Asn Lys His Gly Ile Ile Gly Ala Ser Asn Cys Gly Cys
 1              5              10              15

Ala Ser Asp Asp Val Ala Lys Tyr Pro Leu Ala Asn Asn Pro Tyr Ser
 20              25              30

Ser Ala Leu Asn Leu Asn Ser Cys Gln Asn Ser Ser Ile Leu Asn Trp
 35              40              45

Ile Asn Ile Ile Gly Asp Ala Ala Lys Glu Ala Val Ser Ile Gly Thr
 50              55              60

Thr Ile Val Ser Leu Ile Thr Ala Pro Ser Leu Thr Gly Leu Ile Ser
 65              70              75              80

Ile Val Tyr Asp Leu Ile Gly Lys Val Leu Gly Gly Ser Ser Gly Gln
 85              90              95

Ser Ile Ser Asp Leu Ser Ile Cys Asp Leu Leu Ser Ile Ile Asp Leu
100              105              110

Arg Val Ser Gln Ser Val Leu Asn Asp Gly Ile Ala Asp Phe Asn Gly
115              120              125

Ser Val Leu Leu Tyr Arg Asn Tyr Leu Glu Ala Leu Asp Ser Trp Asn
130              135              140

Lys Asn Pro Asn Ser Ala Ser Ala Glu Glu Leu Arg Thr Arg Phe Arg
145              150              155              160

Ile Ala Asp Ser Glu Phe Asp Arg Ile Leu Thr Arg Gly Ser Leu Thr
165              170              175

Asn Gly Gly Ser Leu Ala Arg Gln Asn Ala Gln Ile Leu Leu Leu Pro
180              185              190

Ser Phe Ala Ser Ala Ala Phe Phe His Leu Leu Leu Leu Arg Asp Ala
195              200              205

Thr Arg Tyr Gly Thr Asn Trp Gly Leu Tyr Asn Ala Thr Pro Phe Ile
210              215              220

Asn Tyr Gln Ser Lys Leu Val Glu Leu Ile Glu Leu Tyr Thr Asp Tyr

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Asn Thr Ile Asn Pro Asp Arg Ile Thr Gln Ile Pro Leu Thr Lys Val
 515 520 525
 Asp Thr Arg Gly Thr Gly Val Ser Tyr Val Asn Asp Pro Gly Phe Ile
 530 535 540
 Gly Gly Ala Leu Leu Gln Arg Thr Asp His Gly Ser Leu Gly Val Leu
 545 550 555 560
 Arg Val Gln Phe Pro Leu His Leu Arg Gln Gln Tyr Arg Ile Arg Val
 565 570 575
 Arg Tyr Ala Ser Thr Thr Asn Ile Arg Leu Ser Val Asn Gly Ser Phe
 580 585 590
 Gly Thr Ile Ser Gln Asn Leu Pro Ser Thr Met Arg Leu Gly Glu Asp
 595 600 605
 Leu Arg Tyr Gly Ser Phe Ala Ile Arg Glu Phe Asn Thr Ser Ile Arg
 610 615 620
 Pro Thr Ala Ser Pro Asp Gln Ile Arg Leu Thr Ile Glu Pro Ser Phe
 625 630 635 640
 Ile Arg Gln Glu Val Tyr Val Asp Arg Ile Glu Phe Ile Pro Val Asn
 645 650 655
 Pro Thr Arg Glu Ala Lys Glu Asp Leu Glu Ala Ala Lys Lys Ala Val
 660 665 670
 Ala Ser Leu Phe Thr Arg Thr Arg Asp Gly Leu Gln Val Asn Val Lys
 675 680 685
 Asp Tyr Gln Val Asp Gln Ala Ala Asn Leu Val Ser Cys Leu Ser Asp
 690 695 700
 Glu Gln Tyr Gly Tyr Asp Lys Lys Met Leu Leu Glu Ala Val Arg Ala
 705 710 715 720
 Ala Lys Arg Leu Ser Arg Glu Arg Asn Leu Leu Gln Asp Pro Asp Phe
 725 730 735
 Asn Thr Ile Asn Ser Thr Glu Glu Asn Gly Trp Lys Ala Ser Asn Gly
 740 745 750
 Val Thr Ile Ser Glu Gly Gly Pro Phe Tyr Lys Gly Arg Ala Ile Gln
 755 760 765
 Leu Ala Ser Ala Arg Glu Asn Tyr Pro Thr Tyr Ile Tyr Gln Lys Val
 770 775 780
 Asp Ala Ser Glu Leu Lys Pro Tyr Thr Arg Tyr Arg Leu Asp Gly Phe
 785 790 795 800

Val Lys Ser Ser Gln Asp Leu Glu Ile Asp Leu Ile His His His Lys
 805 810 815
 Val His Leu Val Lys Asn Val Pro Asp Asn Leu Val Ser Asp Thr Tyr
 820 825 830
 Pro Asp Asp Ser Cys Ser Gly Ile Asn Arg Cys Gln Glu Gln Gln Met
 835 840 845
 Val Asn Ala Gln Leu Glu Thr Glu His His His Pro Met Asp Cys Cys
 850 855 860
 Glu Ala Ala Gln Thr His Glu Phe Ser Ser Tyr Ile Asp Thr Gly Asp
 865 870 875 880
 Leu Asn Ser Ser Val Asp Gln Gly Ile Trp Ala Ile Phe Lys Val Arg
 885 890 895
 Thr Thr Asp Gly Tyr Ala Thr Leu Gly Asn Leu Glu Leu Val Glu Val
 900 905 910
 Gly Pro Leu Ser Gly Glu Ser Leu Glu Arg Glu Gln Arg Asp Asn Thr
 915 920 925
 Lys Trp Ser Ala Glu Leu Gly Arg Lys Arg Ala Glu Thr Asp Arg Val
 930 935 940
 Tyr Gln Asp Ala Lys Gln Ser Ile Asn His Leu Phe Val Asp Tyr Gln
 945 950 955 960
 Asp Gln Gln Leu Asn Pro Glu Ile Gly Met Ala Asp Ile Met Asp Ala
 965 970 975
 Gln Asn Leu Val Ala Ser Ile Ser Asp Val Tyr Ser Asp Ala Val Leu
 980 985 990
 Gln Ile Pro Gly Ile Asn Tyr Glu Ile Tyr Thr Glu Leu Ser Asn Arg
 995 1000 1005
 Leu Gln Gln Ala Ser Tyr Leu Tyr Thr Ser Arg Asn Ala Val Gln Asn
 1010 1015 1020
 Gly Asp Phe Asn Asn Gly Leu Asp Ser Trp Asn Ala Thr Ala Gly Ala
 1025 1030 1035 1040
 Ser Val Gln Gln Asp Gly Asn Thr His Phe Leu Val Leu Ser His Trp
 1045 1050 1055
 Asp Ala Gln Val Ser Gln Gln Phe Arg Val Gln Pro Asn Cys Lys Tyr
 1060 1065 1070
 Val Leu Arg Val Thr Ala Glu Lys Val Gly Gly Gly Asp Gly Tyr Val

| | | |
|---|------|-----------|
| 1075 | 1080 | 1085 |
| Thr Ile Arg Asp Asp Ala His His Thr Glu Thr Leu Thr Phe Asn Ala | | |
| 1090 | 1095 | 1100 |
| Cys Asp Tyr Asp Ile Asn Gly Thr Tyr Val Thr Asp Asn Thr Tyr Leu | | |
| 1105 | 1110 | 1115 1120 |
| Thr Lys Glu Val Val Phe His Pro Glu Thr Gln His Met Trp Val Glu | | |
| | 1125 | 1130 1135 |
| Val Asn Glu Thr Glu Gly Ala Phe His Ile Asp Ser Ile Glu Phe Val | | |
| | 1140 | 1145 1150 |
| Glu Thr Glu Lys | | |
| 1155 | | |

(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 3726 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..3726

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

| | |
|---|-----|
| ATG AAT CAA AAT AAA CAC GGA ATT ATT GGC GCT TCC AAT TGT GGT TGT | 48 |
| Met Asn Gln Asn Lys His Gly Ile Ile Gly Ala Ser Asn Cys Gly Cys | |
| 1 5 10 15 | |
| GCA TCT GAT GAT GTT GCG AAA TAT CCT TTA GCC AAC AAT CCA TAT TCA | 96 |
| Ala Ser Asp Asp Val Ala Lys Tyr Pro Leu Ala Asn Asn Pro Tyr Ser | |
| 20 25 30 | |
| TCT GCT TTA AAT TTA AAT TCT TGT CAA AAT AGT AGT ATT CTC AAC TGG | 144 |
| Ser Ala Leu Asn Leu Asn Ser Cys Gln Asn Ser Ser Ile Leu Asn Trp | |
| 35 40 45 | |
| ATT AAC ATA ATA GGC GAT GCA GCA AAA GAA GCA GTA TCT ATT GGG ACA | 192 |
| Ile Asn Ile Ile Gly Asp Ala Ala Lys Glu Ala Val Ser Ile Gly Thr | |
| 50 55 60 | |
| ACC ATA GTC TCT CTT ATC ACA GCA CCT TCT CTT ACT GGA TTA ATT TCA | 240 |

75

| 275 | 280 | 285 | |
|---|-----|-----|------|
| ACT AAT TAC CCA ATA GAA ACA GAT TTT CAG TTG AGT AGG GTC ATT TAT | | | 912 |
| Thr Asn Tyr Pro Ile Glu Thr Asp Phe Gln Leu Ser Arg Val Ile Tyr | | | |
| 290 | 295 | 300 | |
| ACA GAT CCA ATT GGT TTT GTA CAT CGT AGT AGT CTT AGG GGA GAA AGT | | | 960 |
| Thr Asp Pro Ile Gly Phe Val His Arg Ser Ser Leu Arg Gly Glu Ser | | | |
| 305 | 310 | 315 | 320 |
| TGG TTT AGC TTT GTT AAT AGA GCT AAT TTC TCA GAT TTA GAA AAT GCA | | | 1008 |
| Trp Phe Ser Phe Val Asn Arg Ala Asn Phe Ser Asp Leu Glu Asn Ala | | | |
| | 325 | 330 | 335 |
| ATA CCT AAT CCT AGA CCG TCT TGG TTT TTA AAT AAT ATG ATT ATA TCT | | | 1056 |
| Ile Pro Asn Pro Arg Pro Ser Trp Phe Leu Asn Asn Met Ile Ile Ser | | | |
| | 340 | 345 | 350 |
| ACT GGT TCA CTT ACA TTG CCG GTT AGC CCA AGT ACT GAT AGA GCG AGG | | | 1104 |
| Thr Gly Ser Leu Thr Leu Pro Val Ser Pro Ser Thr Asp Arg Ala Arg | | | |
| | 355 | 360 | 365 |
| GTA TGG TAT GGA AGT CGA GAT CGA ATT TCC CCT GCT AAT TCA CAA TTT | | | 1152 |
| Val Trp Tyr Gly Ser Arg Asp Arg Ile Ser Pro Ala Asn Ser Gln Phe | | | |
| | 370 | 375 | 380 |
| ATT ACT GAA CTA ATC TCT GGA CAA CAT ACG ACT GCT ACA CAA ACT ATT | | | 1200 |
| Ile Thr Glu Leu Ile Ser Gly Gln His Thr Thr Ala Thr Gln Thr Ile | | | |
| 385 | 390 | 395 | 400 |
| TTA GGG CGA AAT ATA TTT AGA GTA GAT TCT CAA GCT TGT AAT TTA AAT | | | 1248 |
| Leu Gly Arg Asn Ile Phe Arg Val Asp Ser Gln Ala Cys Asn Leu Asn | | | |
| | 405 | 410 | 415 |
| GAT ACC ACA TAT GGA GTG AAT AGG GCG GTA TTT TAT CAT GAT GCG AGT | | | 1296 |
| Asp Thr Thr Tyr Gly Val Asn Arg Ala Val Phe Tyr His Asp Ala Ser | | | |
| | 420 | 425 | 430 |
| GAA GGT TCT CAA AGA TCC GTG TAC GAG GGG TAT ATT CGA ACA ACT GGG | | | 1344 |
| Glu Gly Ser Gln Arg Ser Val Tyr Glu Gly Tyr Ile Arg Thr Thr Gly | | | |
| | 435 | 440 | 445 |
| ATA GAT AAC CCT AGA GTT CAA AAT ATT AAC ACT TAT TTA CCT GGA GAA | | | 1392 |
| Ile Asp Asn Pro Arg Val Gln Asn Ile Asn Thr Tyr Leu Pro Gly Glu | | | |
| | 450 | 455 | 460 |
| AAT TCA GAT ATC CCA ACT CCA GAA GAC TAT ACT CAT ATA TTA AGC ACA | | | 1440 |
| Asn Ser Asp Ile Pro Thr Pro Glu Asp Tyr Thr His Ile Leu Ser Thr | | | |
| 465 | 470 | 475 | 480 |
| ACA ATA AAT TTA ACA GGA GGA CTT AGA CAA GTA GCA TCT AAT CGC CGT | | | 1488 |
| Thr Ile Asn Leu Thr Gly Gly Leu Arg Gln Val Ala Ser Asn Arg Arg | | | |
| | 485 | 490 | 495 |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| TCA | TCT | TTA | GTA | ATG | TAT | GGT | TGG | ACA | CAT | AAA | AGT | CTG | GCT | CGT | AAC | 1536 |
| Ser | Ser | Leu | Val | Met | Tyr | Gly | Trp | Thr | His | Lys | Ser | Leu | Ala | Arg | Asn | |
| | | 500 | | | | | 505 | | | | | 510 | | | | |
| AAT | ACC | ATT | AAT | CCA | GAT | AGA | ATT | ACA | CAG | ATA | CCT | TTA | GTG | AAA | GGA | 1584 |
| Asn | Thr | Ile | Asn | Pro | Asp | Arg | Ile | Thr | Gln | Ile | Pro | Leu | Val | Lys | Gly | |
| | | 515 | | | | | 520 | | | | | 525 | | | | |
| TTT | AGA | GTT | TGG | GGG | GGC | ACC | TCT | GTC | ATT | ACA | GGA | CCA | GGA | TTT | ACA | 1632 |
| Phe | Arg | Val | Trp | Gly | Gly | Thr | Ser | Val | Ile | Thr | Gly | Pro | Gly | Phe | Thr | |
| | 530 | | | | | 535 | | | | | 540 | | | | | |
| GGA | GGG | GAT | ATC | CTT | CGA | AGA | AAT | ACC | TTT | GGT | GAT | TTT | GTA | TCT | CTA | 1680 |
| Gly | Gly | Asp | Ile | Leu | Arg | Arg | Asn | Thr | Phe | Gly | Asp | Phe | Val | Ser | Leu | |
| 545 | | | | | 550 | | | | | 555 | | | | | 560 | |
| CAA | GTC | AAT | ATT | AAT | TCA | CCA | ATT | ACC | CAA | AGA | TAC | CGT | TTA | AGA | TTT | 1728 |
| Gln | Val | Asn | Ile | Asn | Ser | Pro | Ile | Thr | Gln | Arg | Tyr | Arg | Leu | Arg | Phe | |
| | | | | 565 | | | | | 570 | | | | | 575 | | |
| CGT | TAC | GCT | TCC | AGT | AGG | GAT | GCA | CGA | GTT | ATA | GTA | TTA | ACA | GGA | GCG | 1776 |
| Arg | Tyr | Ala | Ser | Ser | Arg | Asp | Ala | Arg | Val | Ile | Val | Leu | Thr | Gly | Ala | |
| | | | 580 | | | | | 585 | | | | | 590 | | | |
| GCA | TCC | ACA | GGA | GTG | GGA | GGC | CAA | GTT | AGT | GTA | AAT | ATG | CCT | CTT | CAG | 1824 |
| Ala | Ser | Thr | Gly | Val | Gly | Gly | Gln | Val | Ser | Val | Asn | Met | Pro | Leu | Gln | |
| | | 595 | | | | | 600 | | | | | 605 | | | | |
| AAA | ACT | ATG | GAA | ATA | GGG | GAG | AAC | TTA | ACA | TCT | AGA | ACA | TTT | AGA | TAT | 1872 |
| Lys | Thr | Met | Glu | Ile | Gly | Glu | Asn | Leu | Thr | Ser | Arg | Thr | Phe | Arg | Tyr | |
| | 610 | | | | | 615 | | | | | 620 | | | | | |
| ACC | GAT | TTT | AGT | AAT | CCT | TTT | TCA | TTT | AGA | GCT | AAT | CCA | GAT | ATA | ATT | 1920 |
| Thr | Asp | Phe | Ser | Asn | Pro | Phe | Ser | Phe | Arg | Ala | Asn | Pro | Asp | Ile | Ile | |
| | 625 | | | | 630 | | | | | 635 | | | | 640 | | |
| GGG | ATA | AGT | GAA | CAA | CCT | CTA | TTT | GGT | GCA | GGT | TCT | ATT | AGT | AGC | GGT | 1968 |
| Gly | Ile | Ser | Glu | Gln | Pro | Leu | Phe | Gly | Ala | Gly | Ser | Ile | Ser | Ser | Gly | |
| | | | | 645 | | | | | 650 | | | | | 655 | | |
| GAA | CTT | TAT | ATA | GAT | AAA | ATT | GAA | ATT | ATT | CTA | GCA | GAT | GCA | ACA | TTT | 2016 |
| Glu | Leu | Tyr | Ile | Asp | Lys | Ile | Glu | Ile | Ile | Leu | Ala | Asp | Ala | Thr | Phe | |
| | | | 660 | | | | | 665 | | | | | 670 | | | |
| GAA | GCA | GAA | TCT | GAT | TTA | GAA | AGA | GCA | CAA | AAG | GCG | GTG | AAT | GCC | CTG | 2064 |
| Glu | Ala | Glu | Ser | Asp | Leu | Glu | Arg | Ala | Gln | Lys | Ala | Val | Asn | Ala | Leu | |
| | | 675 | | | | | 680 | | | | | 685 | | | | |
| TTT | ACT | TCT | TCC | AAT | CAA | ATC | GGG | TTA | AAA | ACC | GAT | GTG | ACG | GAT | TAT | 2112 |
| Phe | Thr | Ser | Ser | Asn | Gln | Ile | Gly | Leu | Lys | Thr | Asp | Val | Thr | Asp | Tyr | |
| | 690 | | | | | 695 | | | | | 700 | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| CAT | ATT | GAT | CAA | GTA | TCC | AAT | TTA | GTG | GAT | TGT | TTA | TCA | GAT | GAA | TTT | 2160 |
| His | Ile | Asp | Gln | Val | Ser | Asn | Leu | Val | Asp | Cys | Leu | Ser | Asp | Glu | Phe | |
| 705 | | | | | 710 | | | | 715 | | | | | 720 | | |
| TGT | CTG | GAT | GAA | AAG | CGA | GAA | TTG | TCC | GAG | AAA | GTC | AAA | CAT | GCG | AAG | 2208 |
| Cys | Leu | Asp | Glu | Lys | Arg | Glu | Leu | Ser | Glu | Lys | Val | Lys | His | Ala | Lys | |
| | | | | 725 | | | | | 730 | | | | | 735 | | |
| CGA | CTC | AGT | GAT | GAG | CGG | AAT | TTA | CTT | CAA | GAT | CCA | AAC | TTC | AGA | GGG | 2256 |
| Arg | Leu | Ser | Asp | Glu | Arg | Asn | Leu | Leu | Gln | Asp | Pro | Asn | Phe | Arg | Gly | |
| | | | 740 | | | | | | 745 | | | | | 750 | | |
| ATC | AAT | AGA | CAA | CCA | GAC | CGT | GGC | TGG | AGA | GGA | AGT | ACA | GAT | ATT | ACC | 2304 |
| Ile | Asn | Arg | Gln | Pro | Asp | Arg | Gly | Trp | Arg | Gly | Ser | Thr | Asp | Ile | Thr | |
| | | 755 | | | | | 760 | | | | | 765 | | | | |
| ATC | CAA | GGA | GGA | GAT | GAC | GTA | TTC | AAA | GAG | AAT | TAC | GTC | ACA | CTA | CCG | 2352 |
| Ile | Gln | Gly | Gly | Asp | Asp | Val | Phe | Lys | Glu | Asn | Tyr | Val | Thr | Leu | Pro | |
| | | 770 | | | | | 775 | | | | 780 | | | | | |
| GGT | ACC | GTT | GAT | GAG | TGC | TAT | CCA | ACG | TAT | TTA | TAT | CAG | AAA | ATA | GAT | 2400 |
| Gly | Thr | Val | Asp | Glu | Cys | Tyr | Pro | Thr | Tyr | Leu | Tyr | Gln | Lys | Ile | Asp | |
| 785 | | | | | 790 | | | | | 795 | | | | 800 | | |
| GAG | TCG | AAA | TTA | AAA | GCT | TAT | ACC | CGT | TAT | GAA | TTA | AGA | GGG | TAT | ATC | 2448 |
| Glu | Ser | Lys | Leu | Lys | Ala | Tyr | Thr | Arg | Tyr | Glu | Leu | Arg | Gly | Tyr | Ile | |
| | | | | 805 | | | | | 810 | | | | | 815 | | |
| GAA | GAT | AGT | CAA | GAC | TTA | GAA | ATC | TAT | TTG | ATC | CGT | TAC | AAT | GCA | AAA | 2496 |
| Glu | Asp | Ser | Gln | Asp | Leu | Glu | Ile | Tyr | Leu | Ile | Arg | Tyr | Asn | Ala | Lys | |
| | | | 820 | | | | | 825 | | | | | 830 | | | |
| CAC | GAA | ATA | GTA | AAT | GTG | CCA | GGC | ACG | GGT | TCC | TTA | TGG | CCG | CTT | TCA | 2544 |
| His | Glu | Ile | Val | Asn | Val | Pro | Gly | Thr | Gly | Ser | Leu | Trp | Pro | Leu | Ser | |
| | | 835 | | | | | 840 | | | | | 845 | | | | |
| GCC | CAA | AGT | CCA | ATC | GGA | AAG | TGT | GGA | GAA | CCG | AAT | CGA | TGC | GCG | CCA | 2592 |
| Ala | Gln | Ser | Pro | Ile | Gly | Lys | Cys | Gly | Glu | Pro | Asn | Arg | Cys | Ala | Pro | |
| | | 850 | | | | 855 | | | | | 860 | | | | | |
| CAC | CTT | GAA | TGG | AAT | CCT | GAT | CTA | GAT | TGT | TCC | TGC | AGA | GAC | GGG | GAA | 2640 |
| His | Leu | Glu | Trp | Asn | Pro | Asp | Leu | Asp | Cys | Ser | Cys | Arg | Asp | Gly | Glu | |
| 865 | | | | | 870 | | | | 875 | | | | | 880 | | |
| AAA | TGT | GCA | CAT | CAT | TCC | CAT | CAT | TTC | ACC | TTG | GAT | ATT | GAT | GTT | GGA | 2688 |
| Lys | Cys | Ala | His | His | Ser | His | His | Phe | Thr | Leu | Asp | Ile | Asp | Val | Gly | |
| | | | | 885 | | | | | 890 | | | | | 895 | | |
| TGT | ACA | GAC | TTA | AAT | GAG | GAC | TTA | GGT | GTA | TGG | GTG | ATA | TTC | AAG | ATT | 2736 |
| Cys | Thr | Asp | Leu | Asn | Glu | Asp | Leu | Gly | Val | Trp | Val | Ile | Phe | Lys | Ile | |
| | | | 900 | | | | | 905 | | | | | 910 | | | |
| AAG | ACG | CAA | GAT | GGC | CAT | GCA | AGA | CTA | GGG | AAT | CTA | GAG | TTT | CTC | GAA | 2784 |

| | | | | | | | | | | | | | | | | | |
|-----|-----|------|------|------|-----|------|------|------|------|------|------|------|------|------|------|------|--|
| Lys | Thr | Gln | Asp | Gly | His | Ala | Arg | Leu | Gly | Asn | Leu | Glu | Phe | Leu | Glu | | |
| | | 915 | | | | | 920 | | | | | 925 | | | | | |
| GAG | AAA | CCA | TTA | TTA | GGG | GAA | GCA | CTA | GCT | CGT | GTG | AAA | AGA | GCG | GAG | 2832 | |
| Glu | Lys | Pro | Leu | Leu | Gly | Glu | Ala | Leu | Ala | Arg | Val | Lys | Arg | Ala | Glu | | |
| | | 930 | | | | | 935 | | | | 940 | | | | | | |
| AAG | AAG | TGG | AGA | GAC | AAA | CGA | GAG | AAA | CTG | CAG | TTG | GAA | ACA | AAT | ATT | 2880 | |
| Lys | Lys | Trp | Arg | Asp | Lys | Arg | Glu | Lys | Leu | Gln | Leu | Glu | Thr | Asn | Ile | | |
| | | 945 | | | | 950 | | | | 955 | | | | | 960 | | |
| GTT | TAT | AAA | GAG | GCA | AAA | GAA | TCT | GTA | GAT | GCT | TTA | TTT | GTA | AAC | TCT | 2928 | |
| Val | Tyr | Lys | Glu | Ala | Lys | Glu | Ser | Val | Asp | Ala | Leu | Phe | Val | Asn | Ser | | |
| | | | | 965 | | | | | 970 | | | | | 975 | | | |
| CAA | TAT | GAT | AGA | TTA | CAA | GTG | GAT | ACG | AAC | ATC | GCG | ATG | ATT | CAT | GCG | 2976 | |
| Gln | Tyr | Asp | Arg | Leu | Gln | Val | Asp | Thr | Asn | Ile | Ala | Met | Ile | His | Ala | | |
| | | | 980 | | | | | 985 | | | | | 990 | | | | |
| GCA | GAT | AAA | CGC | GTT | CAT | AGA | ATC | CGG | GAA | GCG | TAT | CTG | CCA | GAG | TTG | 3024 | |
| Ala | Asp | Lys | Arg | Val | His | Arg | Ile | Arg | Glu | Ala | Tyr | Leu | Pro | Glu | Leu | | |
| | | 995 | | | | | 1000 | | | | | 1005 | | | | | |
| TCT | GTG | ATT | CCA | GGT | GTC | AAT | GCG | GCC | ATT | TTC | GAA | GAA | TTA | GAG | GGA | 3072 | |
| Ser | Val | Ile | Pro | Gly | Val | Asn | Ala | Ala | Ile | Phe | Glu | Glu | Leu | Glu | Gly | | |
| | | 1010 | | | | 1015 | | | | | 1020 | | | | | | |
| CGT | ATT | TTT | ACA | GCG | TAT | TCC | TTA | TAT | GAT | GCG | AGA | AAT | GTC | ATT | AAA | 3120 | |
| Arg | Ile | Phe | Thr | Ala | Tyr | Ser | Leu | Tyr | Asp | Ala | Arg | Asn | Val | Ile | Lys | | |
| | | 1025 | | | | 1030 | | | | 1035 | | | | | 1040 | | |
| AAT | GGC | GAT | TTC | AAT | AAT | GGC | TTA | TTA | TGC | TGG | AAC | GTG | AAA | GGT | CAT | 3168 | |
| Asn | Gly | Asp | Phe | Asn | Asn | Gly | Leu | Leu | Cys | Trp | Asn | Val | Lys | Gly | His | | |
| | | | | 1045 | | | | | 1050 | | | | 1055 | | | | |
| GTA | GAT | GTA | GAA | GAG | CAA | AAC | AAC | CAC | CGT | TCG | GTC | CTT | GTT | ATC | CCA | 3216 | |
| Val | Asp | Val | Glu | Glu | Gln | Asn | Asn | His | Arg | Ser | Val | Leu | Val | Ile | Pro | | |
| | | | 1060 | | | | | 1065 | | | | | 1070 | | | | |
| GAA | TGG | GAG | GCA | GAA | GTG | TCA | CAA | GAG | GTT | CGT | GTC | TGT | CCA | GGT | CGT | 3264 | |
| Glu | Trp | Glu | Ala | Glu | Val | Ser | Gln | Glu | Val | Arg | Val | Cys | Pro | Gly | Arg | | |
| | | 1075 | | | | | 1080 | | | | | 1085 | | | | | |
| GGC | TAT | ATC | CTT | CGT | GTC | ACA | GCA | TAT | AAA | GAG | GGA | TAT | GGA | GAG | GGC | 3312 | |
| Gly | Tyr | Ile | Leu | Arg | Val | Thr | Ala | Tyr | Lys | Glu | Gly | Tyr | Gly | Glu | Gly | | |
| | | 1090 | | | | | 1095 | | | | 1100 | | | | | | |
| TGC | GTA | ACG | ATC | CAT | GAG | ATC | GAA | GAC | AAT | ACA | GAC | GAA | CTG | AAA | TTC | 3360 | |
| Cys | Val | Thr | Ile | His | Glu | Ile | Glu | Asp | Asn | Thr | Asp | Glu | Leu | Lys | Phe | | |
| | | 1105 | | | | 1110 | | | | 1115 | | | | 1120 | | | |
| AGC | AAC | TGT | GTA | GAA | GAG | GAA | GTA | TAT | CCA | AAC | AAC | ACA | GTA | ACG | TGT | 3408 | |
| Ser | Asn | Cys | Val | Glu | Glu | Glu | Val | Tyr | Pro | Asn | Asn | Thr | Val | Thr | Cys | | |

| 1125 | 1130 | 1135 | |
|---|------|------|------|
| AAT AAT TAT ACT GGG ACT CAA GAA GAA TAT GAG GGT ACG TAC ACT TCT | | | 3456 |
| Asn Asn Tyr Thr Gly Thr Gln Glu Glu Tyr Glu Gly Thr Tyr Thr Ser | | | |
| 1140 | 1145 | 1150 | |
| CGT AAT CAA GGA TAT GAC GAA GCC TAT GGT AAT AAC CCT TCC GTA CCA | | | 3504 |
| Arg Asn Gln Gly Tyr Asp Glu Ala Tyr Gly Asn Asn Pro Ser Val Pro | | | |
| 1155 | 1160 | 1165 | |
| GCT GAT TAC GCT TCA GTC TAT GAA GAA AAA TCG TAT ACA GAT GGA CGA | | | 3552 |
| Ala Asp Tyr Ala Ser Val Tyr Glu Glu Lys Ser Tyr Thr Asp Gly Arg | | | |
| 1170 | 1175 | 1180 | |
| AGA GAG AAT CCT TGT GAA TCT AAC AGA GGC TAT GGG GAT TAC ACA CCA | | | 3600 |
| Arg Glu Asn Pro Cys Glu Ser Asn Arg Gly Tyr Gly Asp Tyr Thr Pro | | | |
| 1185 | 1190 | 1195 | 1200 |
| CTA CCG GCT GGT TAT GTA ACA AAG GAT TTA GAG TAC TTC CCA GAG ACC | | | 3648 |
| Leu Pro Ala Gly Tyr Val Thr Lys Asp Leu Glu Tyr Phe Pro Glu Thr | | | |
| 1205 | 1210 | 1215 | |
| GAT AAG GTA TGG ATT GAG ATC GGA GAA ACA GAA GGA ACA TTC ATC GTG | | | 3696 |
| Asp Lys Val Trp Ile Glu Ile Gly Glu Thr Glu Gly Thr Phe Ile Val | | | |
| 1220 | 1225 | 1230 | |
| GAT AGC GTG GAA TTA CTC CTT ATG GAG GAA | | | 3726 |
| Asp Ser Val Glu Leu Leu Leu Met Glu Glu | | | |
| 1235 | 1240 | | |

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1242 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Asn | Gln | Asn | Lys | His | Gly | Ile | Ile | Gly | Ala | Ser | Asn | Cys | Gly | Cys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Ala | Ser | Asp | Asp | Val | Ala | Lys | Tyr | Pro | Leu | Ala | Asn | Asn | Pro | Tyr | Ser |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Ser | Ala | Leu | Asn | Leu | Asn | Ser | Cys | Gln | Asn | Ser | Ser | Ile | Leu | Asn | Trp |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Ile | Asn | Ile | Ile | Gly | Asp | Ala | Ala | Lys | Glu | Ala | Val | Ser | Ile | Gly | Thr |
| | 50 | | | | | 55 | | | | | 60 | | | | |

Thr Ile Val Ser Leu Ile Thr Ala Pro Ser Leu Thr Gly Leu Ile Ser
 65 70 75 80
 Ile Val Tyr Asp Leu Ile Gly Lys Val Leu Gly Gly Ser Ser Gly Gln
 85 90 95
 Ser Ile Ser Asp Leu Ser Ile Cys Asp Leu Leu Ser Ile Ile Asp Leu
 100 105 110
 Arg Val Ser Gln Ser Val Leu Asn Asp Gly Ile Ala Asp Phe Asn Gly
 115 120 125
 Ser Val Leu Leu Tyr Arg Asn Tyr Leu Glu Ala Leu Asp Ser Trp Asn
 130 135 140
 Lys Asn Pro Asn Ser Ala Ser Ala Glu Glu Leu Arg Thr Arg Phe Arg
 145 150 155 160
 Ile Ala Asp Ser Glu Phe Asp Arg Ile Leu Thr Arg Gly Ser Leu Thr
 165 170 175
 Asn Gly Gly Ser Leu Ala Arg Gln Asn Ala Gln Ile Leu Leu Leu Pro
 180 185 190
 Ser Phe Ala Ser Ala Ala Phe Phe His Leu Leu Leu Leu Arg Asp Ala
 195 200 205
 Thr Arg Tyr Gly Thr Asn Trp Gly Leu Tyr Asn Ala Thr Pro Phe Ile
 210 215 220
 Asn Tyr Gln Ser Lys Leu Val Glu Leu Ile Glu Leu Tyr Thr Asp Tyr
 225 230 235 240
 Cys Val His Trp Tyr Asn Arg Gly Phe Asn Glu Leu Arg Gln Arg Gly
 245 250 255
 Thr Ser Ala Thr Ala Trp Leu Glu Phe His Arg Tyr Arg Arg Glu Met
 260 265 270
 Thr Leu Met Val Leu Asp Ile Val Ala Ser Phe Ser Ser Leu Asp Ile
 275 280 285
 Thr Asn Tyr Pro Ile Glu Thr Asp Phe Gln Leu Ser Arg Val Ile Tyr
 290 295 300
 Thr Asp Pro Ile Gly Phe Val His Arg Ser Ser Leu Arg Gly Glu Ser
 305 310 315 320
 Trp Phe Ser Phe Val Asn Arg Ala Asn Phe Ser Asp Leu Glu Asn Ala
 325 330 335
 Ile Pro Asn Pro Arg Pro Ser Trp Phe Leu Asn Asn Met Ile Ile Ser

| | | |
|---|-----|-----|
| 340 | 345 | 350 |
| Thr Gly Ser Leu Thr Leu Pro Val Ser Pro Ser Thr Asp Arg Ala Arg | | |
| 355 | 360 | 365 |
| Val Trp Tyr Gly Ser Arg Asp Arg Ile Ser Pro Ala Asn Ser Gln Phe | | |
| 370 | 375 | 380 |
| Ile Thr Glu Leu Ile Ser Gly Gln His Thr Thr Ala Thr Gln Thr Ile | | |
| 385 | 390 | 395 |
| Leu Gly Arg Asn Ile Phe Arg Val Asp Ser Gln Ala Cys Asn Leu Asn | | |
| 405 | 410 | 415 |
| Asp Thr Thr Tyr Gly Val Asn Arg Ala Val Phe Tyr His Asp Ala Ser | | |
| 420 | 425 | 430 |
| Glu Gly Ser Gln Arg Ser Val Tyr Glu Gly Tyr Ile Arg Thr Thr Gly | | |
| 435 | 440 | 445 |
| Ile Asp Asn Pro Arg Val Gln Asn Ile Asn Thr Tyr Leu Pro Gly Glu | | |
| 450 | 455 | 460 |
| Asn Ser Asp Ile Pro Thr Pro Glu Asp Tyr Thr His Ile Leu Ser Thr | | |
| 465 | 470 | 475 |
| Thr Ile Asn Leu Thr Gly Gly Leu Arg Gln Val Ala Ser Asn Arg Arg | | |
| 485 | 490 | 495 |
| Ser Ser Leu Val Met Tyr Gly Trp Thr His Lys Ser Leu Ala Arg Asn | | |
| 500 | 505 | 510 |
| Asn Thr Ile Asn Pro Asp Arg Ile Thr Gln Ile Pro Leu Val Lys Gly | | |
| 515 | 520 | 525 |
| Phe Arg Val Trp Gly Gly Thr Ser Val Ile Thr Gly Pro Gly Phe Thr | | |
| 530 | 535 | 540 |
| Gly Gly Asp Ile Leu Arg Arg Asn Thr Phe Gly Asp Phe Val Ser Leu | | |
| 545 | 550 | 555 |
| Gln Val Asn Ile Asn Ser Pro Ile Thr Gln Arg Tyr Arg Leu Arg Phe | | |
| 565 | 570 | 575 |
| Arg Tyr Ala Ser Ser Arg Asp Ala Arg Val Ile Val Leu Thr Gly Ala | | |
| 580 | 585 | 590 |
| Ala Ser Thr Gly Val Gly Gly Gln Val Ser Val Asn Met Pro Leu Gln | | |
| 595 | 600 | 605 |
| Lys Thr Met Glu Ile Gly Glu Asn Leu Thr Ser Arg Thr Phe Arg Tyr | | |
| 610 | 615 | 620 |

Thr Asp Phe Ser Asn Pro Phe Ser Phe Arg Ala Asn Pro Asp Ile Ile
 625 630 635 640
 Gly Ile Ser Glu Gln Pro Leu Phe Gly Ala Gly Ser Ile Ser Ser Gly
 645 650 655
 Glu Leu Tyr Ile Asp Lys Ile Glu Ile Ile Leu Ala Asp Ala Thr Phe
 660 665 670
 Glu Ala Glu Ser Asp Leu Glu Arg Ala Gln Lys Ala Val Asn Ala Leu
 675 680 685
 Phe Thr Ser Ser Asn Gln Ile Gly Leu Lys Thr Asp Val Thr Asp Tyr
 690 695 700
 His Ile Asp Gln Val Ser Asn Leu Val Asp Cys Leu Ser Asp Glu Phe
 705 710 715 720
 Cys Leu Asp Glu Lys Arg Glu Leu Ser Glu Lys Val Lys His Ala Lys
 725 730 735
 Arg Leu Ser Asp Glu Arg Asn Leu Leu Gln Asp Pro Asn Phe Arg Gly
 740 745 750
 Ile Asn Arg Gln Pro Asp Arg Gly Trp Arg Gly Ser Thr Asp Ile Thr
 755 760 765
 Ile Gln Gly Gly Asp Asp Val Phe Lys Glu Asn Tyr Val Thr Leu Pro
 770 775 780
 Gly Thr Val Asp Glu Cys Tyr Pro Thr Tyr Leu Tyr Gln Lys Ile Asp
 785 790 795 800
 Glu Ser Lys Leu Lys Ala Tyr Thr Arg Tyr Glu Leu Arg Gly Tyr Ile
 805 810 815
 Glu Asp Ser Gln Asp Leu Glu Ile Tyr Leu Ile Arg Tyr Asn Ala Lys
 820 825 830
 His Glu Ile Val Asn Val Pro Gly Thr Gly Ser Leu Trp Pro Leu Ser
 835 840 845
 Ala Gln Ser Pro Ile Gly Lys Cys Gly Glu Pro Asn Arg Cys Ala Pro
 850 855 860
 His Leu Glu Trp Asn Pro Asp Leu Asp Cys Ser Cys Arg Asp Gly Glu
 865 870 875 880
 Lys Cys Ala His His Ser His His Phe Thr Leu Asp Ile Asp Val Gly
 885 890 895
 Cys Thr Asp Leu Asn Glu Asp Leu Gly Val Trp Val Ile Phe Lys Ile
 900 905 910

Lys Thr Gln Asp Gly His Ala Arg Leu Gly Asn Leu Glu Phe Leu Glu
 915 920 925

Glu Lys Pro Leu Leu Gly Glu Ala Leu Ala Arg Val Lys Arg Ala Glu
 930 935 940

Lys Lys Trp Arg Asp Lys Arg Glu Lys Leu Gln Leu Glu Thr Asn Ile
 945 950 955 960

Val Tyr Lys Glu Ala Lys Glu Ser Val Asp Ala Leu Phe Val Asn Ser
 965 970 975

Gln Tyr Asp Arg Leu Gln Val Asp Thr Asn Ile Ala Met Ile His Ala
 980 985 990

Ala Asp Lys Arg Val His Arg Ile Arg Glu Ala Tyr Leu Pro Glu Leu
 995 1000 1005

Ser Val Ile Pro Gly Val Asn Ala Ala Ile Phe Glu Glu Leu Glu Gly
 1010 1015 1020

Arg Ile Phe Thr Ala Tyr Ser Leu Tyr Asp Ala Arg Asn Val Ile Lys
 1025 1030 1035 1040

Asn Gly Asp Phe Asn Asn Gly Leu Leu Cys Trp Asn Val Lys Gly His
 1045 1050 1055

Val Asp Val Glu Glu Gln Asn Asn His Arg Ser Val Leu Val Ile Pro
 1060 1065 1070

Glu Trp Glu Ala Glu Val Ser Gln Glu Val Arg Val Cys Pro Gly Arg
 1075 1080 1085

Gly Tyr Ile Leu Arg Val Thr Ala Tyr Lys Glu Gly Tyr Gly Glu Gly
 1090 1095 1100

Cys Val Thr Ile His Glu Ile Glu Asp Asn Thr Asp Glu Leu Lys Phe
 1105 1110 1115 1120

Ser Asn Cys Val Glu Glu Glu Val Tyr Pro Asn Asn Thr Val Thr Cys
 1125 1130 1135

Asn Asn Tyr Thr Gly Thr Gln Glu Glu Tyr Glu Gly Thr Tyr Thr Ser
 1140 1145 1150

Arg Asn Gln Gly Tyr Asp Glu Ala Tyr Gly Asn Asn Pro Ser Val Pro
 1155 1160 1165

Ala Asp Tyr Ala Ser Val Tyr Glu Glu Lys Ser Tyr Thr Asp Gly Arg
 1170 1175 1180

Arg Glu Asn Pro Cys Glu Ser Asn Arg Gly Tyr Gly Asp Tyr Thr Pro

| | | | |
|---|------|------|------|
| 1185 | 1190 | 1195 | 1200 |
| Leu Pro Ala Gly Tyr Val Thr Lys Asp Leu Glu Tyr Phe Pro Glu Thr | | | |
| 1205 | | 1210 | 1215 |
| Asp Lys Val Trp Ile Glu Ile Gly Glu Thr Glu Gly Thr Phe Ile Val | | | |
| 1220 | 1225 | | 1230 |
| Asp Ser Val Glu Leu Leu Leu Met Glu Glu | | | |
| 1235 | 1240 | | |

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "BglII site downstream of translation termination codon of CryIC."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

ATAAGATCTG TT

12

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 35 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "primer"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

GCTAGCCATG GATCAAAATA AACACGGAAT TATTG

35

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "primer"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

CTGGTCAGAT CTTGAAGTA GAGCTCC

27

CTGGTCAGAT CTTGAAGTA GAGCTCC